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ISAAC HALL MANNING, M. D.

Isaac Hall Manning was born in Pittsboro and was raised in Chatham County. His father was John Manning, the first professor of law at the University of North Carolina. Isaac Manning entered the University of North Carolina in the fall of 1883 and graduated in 1887.

The medical school was very young when Dr. Manning joined its faculty in 1901 as professor of physiology. He had had no special training for this position, but immediately set about preparing himself by working in the physiology laboratories at Chicago and Harvard. This lack of training was the first of many obstacles he surmounted during his long career at the University.

In 1905, when Dr. Whitehead went to the University of Virginia, Dr. Manning was selected as dean of the struggling school. He undertook this added responsibility with great trepidation, but with his usual courage and determination set about improving the staff, the curriculum, and especially the standards of work in the school and the requirements for admission. The fact that none of these students who completed the first two years of medicine in the school failed to transfer is ample proof of the excellent job he did, as is the number of outstanding doctors—his former students—practicing medicine throughout this state. During these years the school's reputation as one of the best two-year medical schools in the country became firmly established among the leading four-year schools of the nation.

The present North Carolina medical care program cannot claim direct origin from Isaac Manning, but it is unquestionably a logical development of his philosophy and of his efforts to improve medical care and medical education.

It can probably be said that North Carolina has produced no clearer medical thinker than Isaac Manning. He had already had a full life when he resigned the deanship in 1933, but he continued to teach physiology until he was retired as Kenan Professor Emeritus.

He was elected president of the State Medical Society in the year 1932. He went at this job just as he had gone at every other job he had ever undertaken. He was tremendously interested in hospitalization, and it was largely through his efforts that the Hospital Saving Association in Chapel Hill, a Blue Cross plan, had its beginning. What he did as chairman and medical director of this organization is a matter of record. Before getting too far into this new work, he spent two months in England and France studying hospitalization. His approach to this problem is reminiscent of the days when he was preparing himself to teach physiology, but it was a young man of 67 who went abroad. One says a "young" man because his brain was just as fertile, his source of original thought was just as active as it was in those early days. Yes, when the record is written, it will be found that Isaac Manning in those closing days of his long and fruitful life did a job that can be put on the pedestal with the other great jobs he had done. However, he was not granted the privilege of carrying his plan for voluntary prepaid hospital and medical care insurance as far as he had hoped. He was stricken with a heart attack in December, 1945, and on February 12, 1946, died at the age of 79.

In so short a space it is impossible to mention all the great things that Isaac Manning accomplished during his long life. He also had his disappointments, but he never

gave up, and no man alive or dead has ever seen his shield reversed. The present great medical building that stands at Chapel Hill, while not built under Dr. Manning's regime, represents part of the architectural plans of a building for which he had worked for many years.

But enough of tangible things. No story of Isaac Manning would be complete which fails to tell something about the humanness of the man. He thought of medicine in terms of people. He was a courteous, kindly, and gentle person. He liked his "boys," and every medical student he ever taught received that classification. In spite of all his administrative problems and difficulties, he always had time to advise and counsel his students in his office or at his home.

At times he expressed fear that doctors' professional charges were too high and standards of performance not high enough. He did not feel that any man should get rich from the practice of medicine; he thought of medicine in terms of the humanities. He felt that medical practice was something close to the spiritual, and should be free to those who were not able to pay. That is why he favored a plan that would make medical care available to every man, woman and child of this great state of ours through prepaid insurance.

Isaac Manning is dead, but for those of us who knew and loved him, his influence and his spirit continue to live. Many of the things he worked for still hover beyond the horizon. To us he has thrown the torch, and by God's grace we will make these things come true!

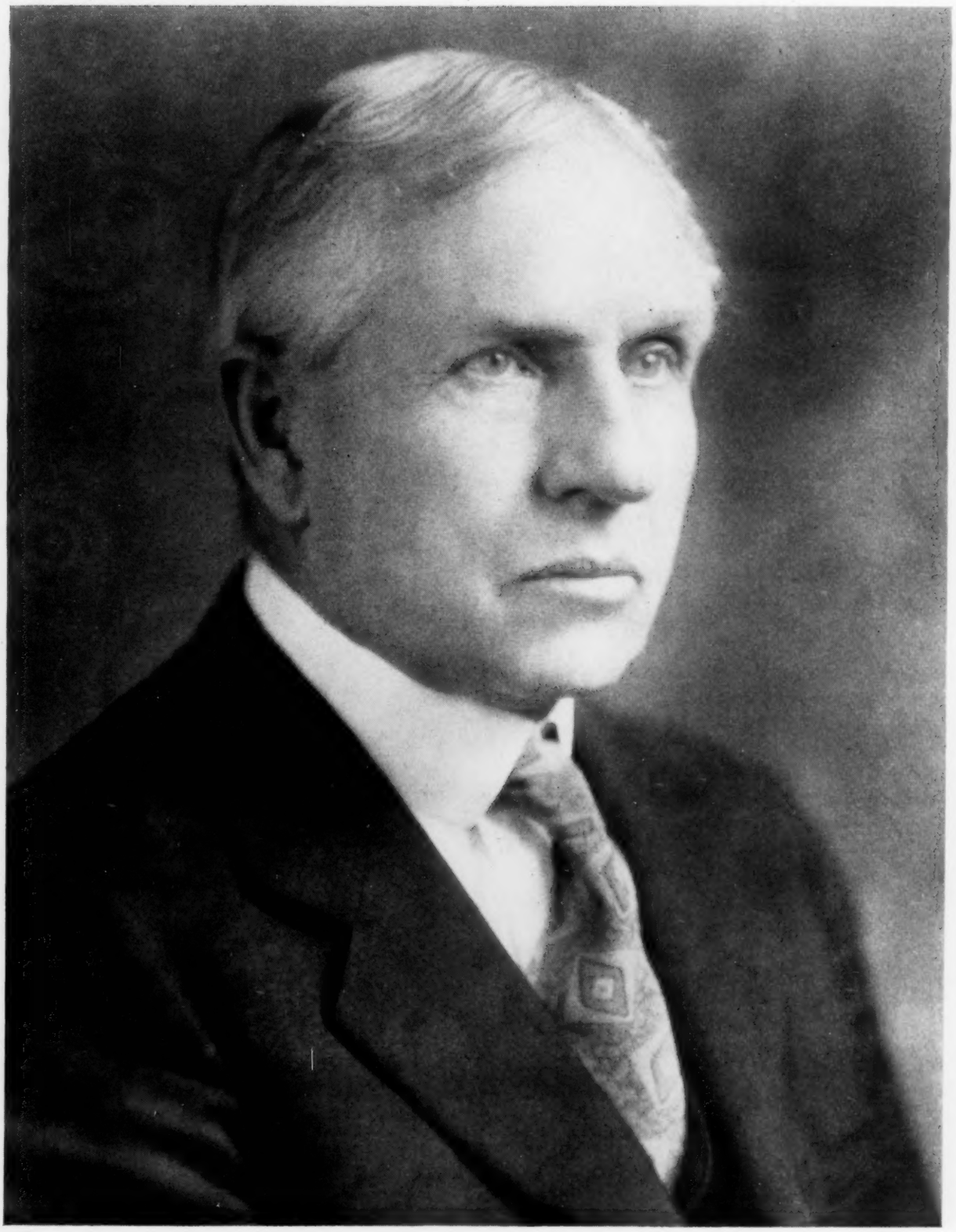
W. Raney Stanford, M.D.
Chief of Medical Service, Watts Hospital, Durham, North Carolina; University of North Carolina Medical School, 1917.

Isaac Hall Manning, son of John and Louisa Hall Manning, was born in Pittsboro, North Carolina, on September 14, 1866, and died in Chapel Hill on February 12, 1946. His family moved to Chapel Hill in 1881, and his father taught in the University's Law School until 1889. After academic study at the University of North Carolina from 1882 to 1886, he served as chemist for the Navasso Guano Company at Wilmington, North Carolina, until 1893, when he entered the medical class at Long Island College, receiving the degree of Doctor of Medicine in 1897. He did graduate work at Harvard and at the University of Chicago, and for a brief period was surgeon for the Atlantic Coast Line Railroad. In 1901 he returned to the University of North Carolina as professor of physiology, a position he held until his retirement as Kenan Emeritus Professor in 1939.

He was married in 1906 to Martha Battle Lewis, who died the following year. In 1911 he married Mary Best Jones, who, with three sons, survives him.

From 1905 to 1933 he was dean of the Medical School. It was during this period and largely through his energy, industry, and sound judgment that this school rose from a position of relative insignificance to one of high esteem in the field of medical education. His personal and intellectual integrity, his high standards of scholarship, his frankness and eminent fairness in all matters brought to him the respect, confidence, and affection of his students and his colleagues, and also brought to this medical school the trust and admiration of the deans and faculties of the other schools to which its students were transferred for their third and fourth years. If one were to make a criticism of his deanship, it would be that his unselfish generosity often led him to starve his own department in order to distribute the school's meager funds more liberally among the other departments. As teacher, administrator, and man he left an ineffaceable stamp upon this state.

Dr. Manning's influence extended far beyond Chapel Hill and the University of North Carolina. The medical profession of the state showed a small measure of its appreciation of his value by making him president of the Medical Society of the State of North Carolina in 1933. In that capacity he did fine service in the interest both of organized medicine and of the general public. It was from his idea and chiefly through his ardent efforts that the Hospital Saving Association was organized. Until his death he continued active direction of this work. This plan of medical and hospital insurance has spread widely throughout the nation and is playing an important part in solving the professional and social needs in matters of medical care.



ISAAC HALL MANNING, M.D.

September 14, 1866 — February 12, 1946

University of North Carolina School of Medicine
Professor of Physiology 1901 - 1939
Dean of School 1905 - 1933

In Dr. Manning's retirement the University lost one of its most useful members; in his death the state lost one of its most useful citizens, and those of us who knew him have lost one of our best friends.

JAMES B. BULLITT, M.D.
Professor of pathology,
University of North Carolina
Medical School.

A simple approach to things was one of Dr. Isaac Hall Manning's characteristics. The superfluous did not appear to bother him. He proceeded directly to the essentials. This ability to reduce things to simple terms has always been one of the attributes of greatness in character, in intelligence, and in science. Dr. Manning possessed the attribute in all three fields.

His character was founded upon the rock of honesty. His intelligence analyzed the medical care problem in North Carolina and combined the component interests of public, hospitals, and physicians into the Hospital Saving Association.

GEORGE L. CARRINGTON, M.D.
Burlington.

THE ATOMIC BOMB EXPERIMENTS IN THE PACIFIC

With a Consideration of the Relationship of Atomic Energy to the Future of Medicine

EUGENE P. PENDERGRASS, M.D.*
PHILADELPHIA

Last summer in the tiny Marshall Island atoll of Bikini two tests were made, Test Able being the detonation of an atomic bomb above the water on July 1 and Test Baker the explosion of another atomic bomb under the water of the lagoon on July 25.

Purpose of Experiments

The purpose of the tests was simple and logical. The atomic bomb is a device utilizing the phenomena of nuclear fission to produce an explosion. The explosion is unparalleled in its magnitude. A great deal of our knowledge concerning the bomb's power and characteristics has been assembled as a result of studies following the explosions at New Mexico, Hiroshima, and Nagasaki, but there is a considerable amount of further information to be obtained. It was with this idea of obtaining more information—some military and some scientific—that the "Operation Crossroads" was planned.

Operation Crossroads was a tremendous enterprise. The job of assembling, operating, and supplying the ships and men involved in the test was in itself an undertaking which compared in size and complexity with a major wartime operation[1]. Approximately 42,000 men and 250 ships participated in the operation[1]. In addition, it was necessary to plan for the gathering and recording of the results of the tests, in order that those observations might be evaluated.

Colonel Stafford Warren of the Manhattan Engineer District was in charge of the protection of personnel from radiologic hazards. Under his direction there were a number of physicists, chemists, engineers, instrument men, and some civilian personnel. Colonel Warren's influence was felt everywhere. There was scarcely a single operation in which he was not directly concerned, because the safety of the personnel was paramount.

The target ships included some of our proud fighting ships with valiant war records. Included in the target array were destroyers, submarines, attack transports, landing ship tanks, landing craft infantry, LCT's, LCM's, floating dry docks, barges, cruisers, aircraft carriers, and battleships. These target vessels were strategically concentrated in the lagoon in the immediate vicinity of the "bull's eye" in order to test the effect of the bomb on the various types of vessels. The detailed knowledge of the destructive power of the bomb should provide the Navy with information concerning any necessary change in ship designs, in tactical formations at sea, and in the manner of anchoring ships in port. Other information was obtained concerning the effect of the atomic bomb against aircraft, both airborne and grounded, and its effect on a wide variety of weapons and equipment.

An important consideration in the test was the effect of the irradiation on living beings. It was necessary to obtain this information in order to know how to provide for the protection and treatment of personnel who may in the future be exposed to atomic bomb radiations, either in war or in peace.

* Professor of radiology, University of Pennsylvania School of Medicine; University of North Carolina Medical School, 1946.

1. "At the Crossroads:" All Hands, pages 2-10, July 1, 1946.

It is recalled that in the New Mexico explosion of the atom bomb, temperatures of fantastic proportions crumpled a steel tower. On the basis of that experiment it was predicted that the terrific blast of heat would undoubtedly cause considerable damage in the immediate vicinity of the detonation. Those of you who have seen movies of the Able test are familiar with the damage that was created as a result of direct heat radiation, and the secondary damage due to explosions of ammunition, gasoline, and other inflammables.

In the two Japanese explosions direct heat radiation was responsible for many casualties. The much publicized radioactive after-effects also caused many deaths and injuries. From the Bikini test, knowledge was obtained concerning the relationship between the distance from the blast and the degree of injury, and also concerning the efficacy of protection offered by steel plates. Information was also obtained on the possibility that radioactive material might enter protected spaces through ventilation ducts.

Many of you will recall the predictions concerning water disturbances which would be caused by the under-water detonation of the bomb. These predictions varied from conservative 70-foot waves in the immediate vicinity of the explosion, to horrifying visions of bomb-born tidal waves, engulfing cities on distant shorelines. It was foreseen that ships near the explosion center would be subjected to terrific stresses, but it was not until after the Bikini test blast that the real information was obtained.

Description of Operation Crossroads

The island of Bikini was transformed into a robot laboratory, in which automatic cameras and devices of various types recorded scientific data concerned with the explosion. The work on Bikini Island was performed by the Fifty-Third Seabee Battalion, veterans of Guadalcanal, Vella Lavella, Bougainville, and Guam[1].

Able test

The lagoon, which is about ten miles wide and twenty miles long, is about the size of San Francisco Bay. It was divided into sectors, and the target ships were placed within these sectors. On the day before the Able test the ships of the fleet, except for the target vessels, left the lagoon and took up prescribed stations. These stations were approximately twenty miles away from the target area. Even at that distance we were warned it was not safe to look at the flash of the exploding bomb. On Able day the weather was perfect. There was good visibility and a constant air movement. Therefore, the test proceeded according to plans. Aircraft of the task force were the first to enter the lagoon after the blast, because it was expected that the air would become free of radioactive particles more rapidly than the water. In a relatively short time, the fleet was ordered to approach the lagoon, carefully testing the water as it advanced. After it had been found safe to re-enter the lagoon, the various patrols began to monitor the sectors assigned to them, and in due time the extent of the radioactivity was outlined.

The amount of information obtained from the tests depended to a considerable extent upon the rapidity with which the monitoring of the lagoon and the target ships could be accomplished, because it was only after such information was obtained that the salvage teams were able to swing into action to control secondary fires and internal explosions. Likewise, it was essential that boarding parties return to the ships as soon as it was safe, in order to collect the animals from the ships, remove the scientific instruments, and observe the effect of the bomb on the ships and their equipment. This was a tremendous undertaking, and one of the most important of the entire operation. Three weeks were allotted to the collection of these data.

Baker test

The same general plan was carried out for the Baker test, except that this time it was unnecessary for the fleet to be so far away, and it was possible to look at the blast without injury to the eyes. Following the detonation of the bomb the fleet entered the lagoon more slowly than after the first test. The Baker test was a much more serious undertaking than I had conceived it to be. The radioactivity was more intense, and it was necessary to exert a greater degree of vigilance in order to protect the personnel of the fleet.

The operation is still being carried on, and there is a tremendous amount of work yet to be done. Some of the ships are still radioactive and probably will be for some time to come.

The first two tests at the Crossroads, to my mind, represented the greatest pageant of all times. The fantastic nature of the physical forces brought into play, the mighty effects of radiation, and the tremendous array of ships and men concerned with this test were most impressive.

Effects on Experimental Animals[2]

Able test

A total of about 3500 animals—goats, pigs, guinea pigs, mice from the National Cancer Institute, and albino rats—were dispersed upon twenty-two ships of the target fleet and exposed to the effects of the "Able" bomb. They were tethered, caged, or confined at locations above and below decks.

Ten per cent—about 350—died almost instantly of air blast or heat or both. Fifteen per cent—something over 500—died within a few days from radiation poisoning. Another 350, about half of which would surely have died in any case, were killed for purposes of study. In other words, just about one third of the animals, scattered over an area at least two miles in radius, were the direct victims of the bomb's major effects; yet the Able test, you will recall, was the test which generally was conceded to be the least destructive of the three planned.

Since, in the case of an air burst, the area of lethal radioactivity substantially exceeds the radius of air blast and heat, all of the animals which died may be counted actual or probable victims of radiation effects.

There are two groups of animals surviving the "Able" bomb which are of interest.

The first was a group of 15 goats selected for intensive treatment of radiation sickness. These goats were retrieved from ships on which all others of their breed were dead, each surviving goat from a different ship. One of them was destroyed because of extensive flash burns of the face. Of the remaining 14 goats, 8 died within a period of nine to fifteen days, 1 on the forty-third day, and 1 on the seventy-ninth day. Only four were alive in November, 1946.

As soon as the goats could be received aboard the animal ship and blood counts made, each received a transfusion of whole blood amounting to 15 per cent of the blood volume. Each of the surviving goats received a daily transfusion of whole blood averaging between 7,000 and 8,000 cc. Each was injected with a total of 37,500,000 units of penicillin. The total amount of whole blood which each received amounted to something over 150 gallons.

Ten of the dead goats received a daily average of from 300 to 7200 cc. of whole blood; the total amount of penicillin which each received varied from 1,000,000 to 36,000,000 units.

The four surviving goats are both anemic and leukopenic. Blood analyses made about two weeks after treatment was begun revealed the presence of a few very immature blood cells, but in November there was no acceptable evidence of any regeneration of the blood elements.

The second group comprises about 100 white rats. Every rat in this group is in a leukemoid state. Premature deaths have been occurring regularly in this group, all of which were exposed to intense total radiation. The normal average white cell count of rats in the Crossroads colony was 10,200. This particular group of 100 have—and have had since recapture—white cell counts between 20,000 and 30,000, with an occasional one up to 50,000. It is not known yet whether these rats are in a leukemoid state or whether they have developed a true leukemia.

It has not yet been possible to make any conclusive genetic studies, although both the mice—which were deliberately placed in positions where they would receive sublethal dosages—and some of the rats have produced litters.

Despite the tremendous amount of laboratory and clinical data already on hand, none of the animal studies have reached the stage of final and binding conclusions. The monumental data sheets, taken from remotely controlled instruments, which exactly registered the heat, blast, and radiation intensity at each animal station, remain to be organized and correlated with the respective test subjects. Literally hundreds of prepared specimens must be subjected to pathologic study.

Baker test

In the second or "Baker" test, 199 albino rats—all progeny more or less remote of the original hardy Wistar strain—and 20 pigs were placed at various sheltered positions aboard ships of the target fleet. The pigs were confined in the sick bays of five target ships, presumably ranging in category from the battleship downward through the carrier

2. McCullough, John: Address at Union League in Philadelphia, October 18, 1946.

and cruiser to the destroyer and relatively thin-hulled attack transport. Not one of the pigs was recovered alive. All were killed by radiation. Some were reached immediately, but the last after a lapse of five days. Of the 199 white rats, 129 were recovered alive. It is important to point out that neither heat nor blast had any important effect upon the animals in this test, which were shielded by hulls, upper works, and bulkheads.

Seventy-one of the 199 white rats were dead of radiation when reached by recapture crews. Ten of the surviving group — of which ten, at least one-half would have died —were killed for study. Of the remaining 118, 61 were alive in October, and deaths were occurring regularly.

Contamination of the Environment by Fission Products

In the first test, only about .005 per cent of the fission elements—the actual disintegration elements of the bomb—was absorbed by the water of the lagoon. Such radiation as was absorbed by the target fleet—and hence by the animals placed on the ships—resulted from instantaneous radiation, measurable in a few millionths of a second.

Quite a different situation existed on July 25. There, about 50 per cent of the fission products were trapped by the water and carried aloft. The major portion of the radioactivity returned to the lagoon to contaminate not only the ships but the water of the lagoon over an area of approximately twenty square miles.

Pathologic Effects of Atomic Blast on Human Beings

Captain Shields Warren has recently reported on the pathologic effects of an instantaneous dose of radiation, as a result of his studies at Hiroshima and Nagasaki[3]. He paints a vivid picture of what can be expected from atomic bomb explosions similar to those observed at Bikini. The pathologic effects were divided into two groups: (1) those produced by heat—primary thermal injury of the flash burn type, and secondary thermal injury due to induced fires; and (2) those produced by radiation. At the time of Captain Warren's study, 80,000 people had died in Hiroshima and 45,000 at Nagasaki.

The characteristic clinical course produced by radiation injury resulting from the atomic bomb explosions may be divided into two stages: The *immediate* effects were weakness, malaise, fever, and often death within forty-eight hours; the *delayed* effects manifested themselves in a variety of ways.

The effect on the blood could be readily followed by the clinical manifestations as well as by the laboratory observations. The patients were divided into three groups. The *first* group were those with marked leukopenia, in which infection, particularly Ludwig's angina, was the outstanding manifestation. A great many of these died in the first three weeks after the bombing. In the second group, which lived from three to five weeks, death was associated with thrombocytopenia and marked depletion of the bone marrow. The skin lesions varied from extensive ecchymoses to purpuric patches and small petechiae. Mucosal hemorrhages occurred everywhere. In the *third* group, there was serious bone marrow damage with anemia. At times the marrow was so depleted that little but reticulo-endothelial cells appeared in the blood.

The effect on the gonads was much more prominent in males than in females. Atrophy of the germinal epithelium of the testis was marked. Suppression of menstruation occurred in some of the high school girls. A recent survey by Colonel James Cooney of the Walter Reed Hospital showed that sterility has become more of a problem than was anticipated. Many flesh burns are still unhealed, and keloid formation is tremendous. A large number of persons still have bone marrow deficiencies. Observations will have to be carried on for many years to learn the total effect of instantaneous exposure such as occurs following detonation of bombs similar to those used in Nagasaki and Bikini.

Medical Uses of Atomic Energy

The discussion thus far has been on the use of atomic energy as an instrument of war. What are some of the prospective medical uses of atomic energy?

Plans are now under way by the Manhattan Engineer District to release a great many radioactive isotopes for medical investigation and treatment. The immediate application of such isotopes to medical problems makes it appear relatively certain that advances in therapeutics, in medical science, in biology, and in chemistry are the greatest peace-time reward which will be associated

3. Warren, S.: The Pathologic Effects of an Instantaneous Dose of Radiation, Cancer Research 6:449-453 (Sept.) 1946.

directly with the next ten years of the "atomic age."

It is stated that the chain-reacting uranium piles, such as those located at Hanford, are sources of neutrons and other radiations equivalent to more than a million cyclotrons[4]. These neutrons, which were used to produce new elements such as plutonium, may also be used to produce in quantity long-lived radioactive carbon and hydrogen[4]. These elements will make it possible for the medical research worker to label with radioactivity those organic compounds that play essential roles in the animal and human body, both in health and disease. Almost every organic chemical entity of possible concern in biology or medicine contains one or both of these elements in key structural positions[4]. Thus, by the proper chemical or, if necessary, biologic synthesis, it will be possible to tag most organic compounds of medical or biologic interest with radioactive labels.

For some years radioactive phosphorus, iron, sodium, iodine, strontium sulfur, and potassium have been among the materials used in medical investigations and treatment. Most of us are familiar with the use of radioactive phosphorus in the treatment of leukemia and polycythemia. Strontium has been used experimentally in the treatment of bone tumors. Iodine has been employed in the investigation of thyroid metabolism, and in the treatment of hyperthyroidism and carcinoma of the thyroid. According to Bale[4], none of these radioactive isotopes are comparable in their usefulness to radioactive carbon or hydrogen in the fields of medical research, since each of the former, if present at all, is usually loosely attached to the key structural group of organic compounds.

Radioactive carbon will have important applications in cancer research, in pharmacology, in biology, in medical therapeutics, and in medicine in general. The study of the metabolism of malignant tumors is one of our foremost problems. Considerable basic research still remains to be done also on aging and the degenerative diseases. Bale, in discussing this general subject, states that we still need to know many fundamental things—for instance, what part of the cell is formed permanently during its early development, and what portion is renewed from metabolites supplied by the bloodstream. We need to know what factors are important in cell and tissue degeneration, and whether we can influence the speed and magnitude of such degeneration in any way. How do the different types of tissue cells in an aging animal differ in their metabolism from cells of the immature and young adult animal?

Comprehensive metabolic studies using the tracer technique should provide a basic foundation of knowledge from which it may be possible to obtain an insight leading to an increasing human adult span of productivity and pleasant existence. Radioactive isotopes are the new tools that are of such fundamental importance, and they will soon see nation-wide and world-wide use.

The Importance of the Atomic Bomb as a Military Weapon

In the World Report for September 17 there is a special editorial on the "atomic bomb" as a military weapon. Some of the points brought out in this editorial are as follows:

The one basic and all-important fact concerning the atomic bomb is that it transcends all previous efforts of mankind in the long history of warfare.

The bomb already has altered and will continue to affect the political and military pattern of the world. The question of control of the bomb is now the subject of negotiation and debate.

The atomic bomb has increased vastly the possibility of devastating attack without declaration of war and of pre-war sabotage on a catastrophic scale.

The destructive capacity of the bomb on land is well known as a result of the explosions over Hiroshima and Nagasaki. Exploded in the air at a selected height, it will destroy all normal land structures and most life within a radius of a mile and a half. There will be an additional area of less damage and an extensive delayed effect largely fatal to life, due to radioactivity.

The first Bikini test determined the effect of an air explosion over a closely concentrated group of vessels at anchor. The results indicated that such a bomb would damage fatally even large war ships within an area of half a mile, and inflict damage to exposed structures on a diminishing scale up to a mile. Exposed personnel in this area would be killed or incapacitated.

The second Bikini test determined the effect of a shallow submerged bomb under a closely concentrated group of vessels at anchor. This underwater explosion indicated that such a bomb would sink or seriously damage even large naval vessels at a distance of 500 yards and damage to less degree other vessels up to 1000 yards. It resulted in extensive and persistent radioactive effects on water and ships.

The atomic bomb as a military weapon will have far-reaching effects on the technique of warfare. It will increase the totality, the complexity, the horror, and the cost of war. It will establish science as an additional defense force of every great nation.

4. Bale, W. F.: Some Prospective Medical Uses of Atomic Energy, J. Am. Pharm. A. (Pract. Pharm. Ed.) 7:81-82 (Feb.) 1946.

Control of Atomic Power

Mr. Bernard M. Baruch has presented the American proposal for international control to the members of the United Nations Atomic Commission. His report met with acclaim from most of the nations except Russia and her satellites. Mr. Andrei Gromyko has presented the Russian proposal for international control. Both of these reports should be studied by all of us.

The problem of how to avert atomic disaster is still very new. Only tentative solutions can be brought forth at this time. One thing is certain, we cannot expect to hold up the peace-time uses of atomic energy, even for security reasons. Fortunately we do have the embryonic organization, the United Nations Council. It is possible for it to grow. There is no other way known at present which can establish effective safeguards against war and mass destruction.

The United States has a great opportunity to assume an aggressive leadership in the formation of a world order of universal law, because of its preeminence in military power.

What can you and I do to assist in the movement of peace? This problem is ours. As you know, atomic energy and atomic bombs are marked "made in the United States." Soon they will be made elsewhere.

We can make it our business to keep informed about atomic energy, and in turn keep our representatives conscious of their obligations to strive for everlasting peace. We can join the movement of the atomic scientists. We can make contributions to help defray the expenses of the propaganda these scientists are fostering. The United States, through the United Nations, must become as aggressive in peace as she was in war. Before the world, we must be united in our aims. Even then the progress will be slow and it may be necessary for us to sacrifice more for peace than for war. Above all, we must not become discouraged.

If we can develop a plan for peace which will succeed, *all nations can have atomic energy and much more.*

Rehabilitation in tuberculosis should begin no later than the day the patient enters the sanatorium, because from the beginning he must know that there is still a future for him. This knowledge acquired early in illness makes a great difference in his morale and his manner of adjustment to a changed way of life.—Herman E. Hilleboe, M.D. and Norvin C. Kiefer, M.D., Pub. Health Rep., Mar. 1, 1946.

EXPERIENCES WITH STREPTOMYCIN THERAPY

Review of Clinical and Laboratory Studies at the Boston City Hospital

H. WILLIAM HARRIS, M. D.*
and
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BOSTON

During the past ten years great strides have been made in the treatment of specific bacterial diseases. Since the introduction and widespread clinical use of the sulfonamide drugs and penicillin, the recovery rates in cases of streptococcal, staphylococcal, pneumococcal, and Neisserian infections have been much improved. Penicillin, however, has little or no value in most of the diseases caused by gram-negative bacilli, and although the sulfonamides are effective to some degree against certain of these infections, more effective agents were obviously to be desired. As a result of the diligent search for such agents, various new antibiotics were discovered; these were shown to inhibit enteric organisms and other gram-negative bacilli, but most of them were too toxic for clinical use[1a].

In 1944, Schatz, Bugie and Waksman[1b] reported the isolation of an antibiotic substance from cultures of Actinomyces griseus. This agent, which they termed streptomycin, was found to be highly effective against various gram-negative and acid-fast bacilli, less active against gram-positive micro-organisms, and relatively inactive against the clostridial group[1].

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Massachusetts.

* University of North Carolina Medical School, 1942.

1. (a) Waksman, S. A., and Schatz, A.: Streptomycin—Origin, Nature and Properties, J. Am. Pharm. A. (Scient. Ed.) 34:273-291 (Nov.) 1945. (b) Schatz, A., Bugie, E., and Waksman, S. A.: Streptomycin, a Substance Exhibiting Antibiotic Activity against Gram-Positive and Gram-Negative Bacteria, Proc. Soc. Exper. Biol. & Med. 55:66-69 (Jan.) 1944. (c) Helmholz, H. F.: The Effect of Streptomycin on Bacteria Commonly Found in Urinary Infections, Proc. Staff Meet., Mayo Clin. 20:357-362 (Oct. 3) 1945. (d) Buggs, C. W., Bronstein, B., Hirshfeld, J. W., and Piling, M. A.: The *in Vitro* Action of Streptomycin on Bacteria, J.A.M.A. 130:64-67 (Jan. 12) 1946. (e) Robinson, H. J., Smith, D. G., and Graessle, O. E.: Chemotherapeutic Properties of Streptomycin, Proc. Soc. Exper. Biol. & Med. 57:226-231 (Nov.) 1944. (f) Schatz, A., and Waksman, S. A.: Effect of Streptomycin and Other Antibiotic Substances upon Mycobacterium tuberculosis and Related Organisms, Proc. Soc. Exper. Biol. & Med. 57:244-248 (Nov.) 1944. (g) Feldman, W. H., Hinshaw, H. C., and Mann, F. C.: Streptomycin in Experimental Tuberculosis, Am. Rev. Tuberc. 52:269-298 (Oct.) 1945.

In this paper we wish to review the results of clinical and laboratory experiences in the treatment of various infections with streptomycin at the Boston City Hospital[2]. Most of the findings reviewed here are presented in detail elsewhere[3].

Absorption and Excretion

Streptomycin is poorly absorbed from the gastrointestinal tract, but it is not destroyed by gastric juice or intestinal enzymes, and high concentrations can be recovered from the feces when a dose is given by mouth. High blood concentrations are rapidly obtained following a parenteral dose, and detectable amounts remain in the blood for six to eight hours, depending upon the amount injected[4]. The drug is excreted chiefly in the urine, where 50 to 70 per cent of the total parenteral dose can be recovered following a single dose[4a,d]. Streptomycin can also be recovered from the peritoneal and pleural fluids after parenteral administration, but the absorption into these cavities is delayed and the levels in these fluids are considerably lower than those in the blood. Little or none of the drug crosses the normal meninges into the cerebrospinal fluid, although low concentrations, usually therapeutically inadequate, may be found in the spinal fluid after administration of the drug to patients with meningitis[4d,5].

Dosage and Administration

Streptomycin is standardized by its antibacterial activity. The S unit, as defined by Waksman[1a] is the minimum amount of material which, when present in 1 millimeter of nutrient media, will just inhibit the growth of a given strain of Escherichia coli. One S unit, however, is essentially equal to 1 microgram of pure streptomycin base, and 1 Gm. is, therefore, equivalent to 1,000,000 units. The doses of the drug given therapeutically, being large, are usually referred to by weight, whereas the levels of the drug in the body fluids and the inhibiting concentrations for bacterial strains, being small, are usually recorded in units or micrograms. In the cases to be presented, streptomycin was administered by intramuscular, intravenous and intrathecal injection, by topical application, and by nebulization. The parenteral dose ranged from 1 to 6 Gm. daily.

Streptomycin Levels and Bacterial Sensitivities

There are various methods by which the streptomycin concentrations in body fluids may be determined[6]. In this laboratory, two-fold dilutions of the body fluid are made in broth, and these are inoculated with 50,000 to 100,000 type A Friedlander's bacilli. The strain used is regularly inhibited by 0.78 units but not by 0.39 units of streptomycin per milliliter. The streptomycin sensitivity of a particular bacterial strain is determined by the addition of a 1:100,000 dilution (containing 50,000 to 100,000 organisms) of the pure culture in broth, to serial broth dilutions of streptomycin. The sensitivity is taken as the minimum concentration in which, after twenty-four hours' incubation, there is neither visible growth nor growth on subculture to streptomycin-free agar.

Numerous reports indicate that different bacteria and different strains of any given bacterial species vary considerably in their sensitivity to streptomycin[1c,7a,b]. Of even greater clinical importance, however, is the tendency for a sensitive bacterial strain to

2. The studies were carried out with the collaboration of Drs. Roderick Murray, Tom F. Paine and Lawrence Kilham, and Dr. Manson Meads participated in some of them. Miss Clare Wilcox assisted in the various laboratory studies.

The streptomycin was provided by the National Research Council from suppiles assigned for clinical investigations recommended by the Committee on Chemotherapeutics and Other Agents. The latter part of these studies was aided by a grant from the United States Public Health Service.

3. (a) Finland, M., et al.: Development of Streptomycin Resistance During Treatment, J.A.M.A. 132:16-21 (Sept. 7) 1946. (b) Harris, H. W., et al.: Streptomycin Treatment of Urinary Tract Infections, with Special Reference to the Use of Alkali, Am. J. Med. 2:229-250, 1947. (c) Paine, T. F., Murray, R., Harris, H. W., and Finland, M.: Streptomycin in the Treatment of Certain Gram-Negative Bacillus Infections of the Central Nervous System, Am. J. M. Sc., in press. (d) Harris, H. W., Murray, R. Paine, T. F., and Finland, M.: Streptomycin Treatment of Pulmonary Infections; Clinical and Bacteriological Studies of 6 Cases, New England J. Med. 236:611-622 (April 24) 1947; (e) Harris, H. W., and Finland, M.: Local Streptomycin Therapy of Ear Infections: Clinical and Bacteriological Observations, to be published.

4. (a) Buggs, C. W., Pilling, M. A., Bronstein, B., and Hirshfeld, J. W.: The Absorption, Distribution and Excretion of Streptomycin in Man, J. Clin. Investigation 25:94-102 (Jan.) 1946. (b) Zintel, H. A., et al.: Studies on Streptomycin in Man. I. Absorption, Distribution, Excretion and Toxicity, Am. J. M. Sc. 210:421-430 (Oct.) 1945. (c) Anderson, D. G., and Jewell, M.: The Absorption, Excretion and Toxicity of Streptomycin in Man, New England J. Med. 233:485-491 (Oct. 25) 1945. (d) Rutstein, D. D., Stebbins, R. B., Cathcart, R. T., and Harvey, R. M.: The Absorption and Excretion of Streptomycin in Human Chronic Typhoid Carriers, J. Clin. Investigation, 24:898-909 (Nov.) 1945.

5. Elias, W. F., and Durso, J.: Blood, Urine and Fecal Levels of Streptomycin in the Treatment of Human Infections of E. typhosa, Science 101:589-591 (June 8) 1945.

6. (a) Waksman, S. A., Bugie, E., and Schatz, A.: Isolation of Antibiotic Substances from Soil Micro-Organisms, with Special Reference to Streptothricin and Streptomycin, Proc. Staff Meet., Mayo Clin. 19:537-548 (Nov. 15) 1944. (b) Heilman, D. H.: A Method or Estimating the Concentration of Streptomycin in Body Fluids, Proc. Staff Meet., Mayo Clin. 20:145-150 (May 16) 1945. (c) Stebbins, R. B., and Robinson, H. J.: A Method for Determination of Streptomycin in Body Fluids, Proc. Soc. Exper. Biol. & Med. 59:255-257 (June) 1945. (d) Forgacs, J., Kornegay, G. B., and Henley, T. F.: Studies on Streptomycin. I. Assay in Body Fluids, J. Lab. & Clin. Med. 31:514-522 (May) 1946.

acquire a high degree of resistance to streptomycin when it is exposed to sublethal concentrations of the antibiotic. This phenomenon may easily be demonstrated *in vitro*, and also occurs in patients during treatment[3a,7].

Clinical Results

Streptomycin has been used at the Boston City Hospital for a variety of diseases. The clinical and bacteriologic results in a small but thoroughly studied group of patients with infections of the urinary tract, central nervous system, bronchopulmonary tract, and ears are included in this review.

Urinary tract infections

Studies were made in 21 adult patients with urinary tract infections who were treated with streptomycin. Most of them had chronic pyelonephritis and cystitis, and all had received sulfonamides, penicillin, methenamine, or mandelic acid without improvement in symptoms, pyuria, or bacilluria. Anatomic abnormalities were demonstrated in 10 instances, but retrograde pyelograms were done in only 11 of these patients. Diminished renal function was found in 7 patients; in 3 of them, it was probably the result of chronic infection, while in the other 4, it was associated with hypertensive cardiovascular diseases. These patients had little fever and few distressing symptoms, but all of them had marked pyuria and bacilluria.

Bacteriology. Cultures of the urine were made for two to three days before streptomycin was started, and cultures were repeated at least daily during treatment. The organisms isolated from pretreatment cultures of the urine were first proved to be susceptible to the action of streptomycin *in vitro*, and in most cases to be inhibited by the concentration of the antibiotic expected in the blood and urine. A variety of different gram-negative bacilli were obtained from these cases. Friedlander's bacilli and some of the strains of Aerobacter aerogenes were the most susceptible, whereas Bacillus proteus and two of the strains of Esch. coli were the most resistant of this group.

Treatment. Most of the patients were given streptomycin by intermittent intramuscular injections, and the total daily dose was 2 to 6 Gm. given in amounts of 0.5 to 1.0 Gm. every four to six hours. An initial intravenous dose of 0.5 to 1.0 Gm. was given to 19 of the patients immediately before the first intramuscular injection. One patient, whose urine contained Streptococcus viridans as well as a gram-negative bacillus, was given intramuscular penicillin, 320,000 units daily, along with the streptomycin.

Results. These cases are divided into two groups. The cases included in groups I and II were comparable, and received similar amounts of streptomycin. The patients in group I[3a] received streptomycin without adjuvant alkali, and the urine was acid before and throughout the course of therapy in 6 of these 7 cases. In 6 patients there was no clinical response, and the pyuria and bacilluria persisted during and after therapy. In 5 of these cases, the organisms recovered from the urine after one to four days of streptomycin treatment showed cultural and biochemical characteristics which were identical with those of the pretreatment strains, except that they were now able to grow well in the presence of 50,000 units of streptomycin. In the sixth case, pyuria diminished and cultures showed no growth on the third and fourth days of therapy, and the reaction of the urine, which was initially infected with *B. proteus*, rapidly changed from alkaline to acid. On the fifth day of treatment, however, pyuria and bacilluria recurred, and the organism recovered on that day and thereafter was a strain of *Esch. coli* which was totally resistant to streptomycin. There

7. (a) Reimann, H. A., Price, A. H., and Elias, W. F.: Streptomycin for Certain Systemic Infections and Its Effects on the Urinary and Fecal Flora, Arch. Int. Med. 76:269-277 (Nov.-Dec.) 1945. (b) Waksman, S. A., Reilly, H. C., and Schatz, A.: Strain Specificity and Production of Antibiotic Substances. V. Strain Resistance of Bacteria to Antibiotic Substances, Especially to Streptomycin, Proc. Nat. Acad. Sc. 31:157-164 (June) 1945. (c) Knop, C. Q.: Experimental Study of the Development of Resistance to Streptomycin by Some Bacteria Commonly Found in Urinary Infections, Proc. Staff Meet., Mayo Clin. 21:273-276 (July 24) 1946. (d) Miller, C. P., and Bohnhoff, M.: Streptomycin Resistance of Gonococci and Meningococci, J.A.M.A. 130:485-488 (Feb 23) 1946. (e) Youmans, G. P., Williston, E. H., Feldman, W. H., and Hinshaw, H. C.: Increase in Resistance of Tubercle Bacilli to Streptomycin: A Preliminary Report, Proc. Staff Meet., Mayo Clin. 21: 126-127 (March 20) 1946. (f) Wolinsky, E., and Steenken, W., Jr., Streptomycin and Penicillin Resistant Staphylococci; Influence of *pH*, Body Fluids on Streptomycin Action, Proc. Soc. Exper. Biol. & Med. 62:162-165 (June) 1946. (g) Alexander, H. E., and Leidy, G.: Influence of Streptomycin on Type b Haemophilus Influenzae, Science 104:101 (Aug. 2) 1946. (h) Klein, M., and Kimmelman, L. J.: The Role of Spontaneous Variants in the Acquisition of Streptomycin Resistance by the Shigellae, J. Bact. 52:471-479 (Oct.) 1946. (i) Graessle, O. E., and Frost, B. M.: Induced *in vitro* Resistance of Staphylococci to Streptomycin and Penicillin, Proc. Soc. Exper. Biol. & Med. 63: 171-175 (Oct.) 1946. (j) Sullivan, M., Stahly, G. L., and Birkeland, J. M.: Reciprocal Sensitivities of Staphylococcus Aureus to Streptomycin, Streptothricin, and Penicillin, Science, 104:397 (Oct. 25) 1946. (k) Herrell, W. E., and Nichols, D. R.: The Clinical Use of Streptomycin: A Study of 45 Cases, Proc. Staff Meet., Mayo Clin. 20:449-462 (Nov. 28) 1945. (l) Bondi, A., Jr., Ottenberg, D., Dietz, C. C., and Brown, C. L.: Streptomycin Therapy in Infection of Urinary Tract: Failure Because of Development of Resistance, J.A.M.A. 132:634 (Nov. 16) 1946. (m) Alexander, H. E., Leidy, G., Rake, G., and Donovick, R.: Hemophilus Influenzae Meningitis Treated with Streptomycin, J.A.M.A. 132:434 (Oct. 26) 1946.

Table 1

Summary of the Results of Streptomycin Treatment in Chronic Urinary Tract Infections, with and without Alkali

Group	*Number of Cases*	*"Cures"*	*Transient Improvement*	*No Improvement*	*Streptomycin Resistance Developed*
I—Treated without alkali	7	1	0	6	6
II—Treated with alkali	14	8	6	0	2*

* In one of these cases the resistant strain was recovered only once after treatment, and subsequent urine cultures were negative. In the other cases, the resistant organism isolated from urine after treatment was different from the one obtained before treatment.

was only 1 case in this group in which the pyuria and bacilluria rapidly cleared and did not return during a four-month follow-up period, in spite of the fact that the urine remained acid throughout the course of treatment.

After observing the unfavorable clinical results in this group, a modification of the therapeutic regimen was agreed upon. Because the activity of streptomycin *in vitro* is known to be much greater in an alkaline than in an acid medium[18,8], an attempt was made to determine whether alkalinization of the urine during streptomycin therapy would increase the effectiveness of treatment and reduce or prevent the development of resistance. The 14 patients in group II were, therefore, given alkali for two to four days before streptomycin was started. The urine was alkalinized by the oral administration of sodium bicarbonate and potassium citrate, the usual dose being 1 Gm. of each six times daily, and the reaction was maintained at a *p*H above 7.0 throughout the period of treatment.

The clinical and bacteriologic results of treatment in the two groups of cases are summarized and compared in table 1. "Cures" (freedom from bacilluria persisting throughout the period of observation) were achieved in 8 of the 14 alkalinized patients. In one patient, treatment with streptomycin was successful, but reinfection of the urinary tract with a new bacterial strain occurred five and a half weeks after therapy. Transient improvement was noted in 5 patients, who had no bacilluria during the administration of streptomycin, but developed a recurrence of infection within two weeks after therapy was concluded. In 4 of these 5 patients the organisms obtained at the time of recurrence showed the presence of new strains, distinct from those isolated before treatment. Some of the new strains were gram-positive bacteria, having varying degrees of sensitivity to streptomycin, but there were also 3 new strains of gram-negative bacilli, 1 from each of 3 patients, and only 1 of them was totally resistant to streptomycin. The other new strains which appeared after the conclusion of treatment showed about the same degrees of sensitivity as pretreatment strains of similar organisms isolated from other patients. In 2 patients there was a recurrence of the strains which had been present in urine cultures before treatment, and in each instance the organisms had remained sensitive to streptomycin.

Comment. A comparison of the results of treatment in these two groups of cases suggests that alkalinization did, indeed, have a favorable influence. Of the 14 patients whose urine was kept alkaline throughout the period of streptomycin therapy, 8 were apparently cured of their infection, whereas only 1 among 7 patients who did not receive alkali was cured by streptomycin therapy. Furthermore, the development of resistance to streptomycin by the infecting organisms was much less frequent when the urine was alkaline. In fact, almost all of the organisms recovered after the streptomycin therapy in this group of patients were different from those obtained before treatment and were susceptible to the antibiotic.

Infections of the central nervous system

Gram-negative bacillus infections of the central nervous system, although infrequent, are usually fatal. Four cases of meningitis and 1 case of an infected meningocele, all caused by gram-positive bacilli and treated with streptomycin, were studied[36].

Two of the patients had meningitis due to Pseudomonas aeruginosa (Bacillus pyocyaneus). One was a 14-year-old epileptic in whom the infection followed a diagnostic lumbar puncture, and the other was an infant with an ulcerated meningocele. Both had failed to respond to intensive treatment with sulfadiazine and penicillin. Streptomycin was given both intramuscularly and intrathecally in these cases. The first patient had a rapid clinical response, and the spinal fluid cultures were negative for Ps. aeruginosa after the fourth day of treatment. The

8. (a) Loo, Y. H., et al.: Assay of Streptomycin by the Paper-Disc Plate Method, J. Bact. 50:701-709 (Dec.) 1945. (b) Abraham, E. P., and Duthie, E. S.: Effect of *p*H of the Medium on Activity of Streptomycin and Penicillin and Other Chemotherapeutic Substances, Lancet 1:455-459 (March 30) 1946.

second patient had a more protracted course and required streptomycin for four weeks. The cerebrospinal fluid eventually became bacteria free, but a left facial paresis occurred during treatment and persisted throughout the follow-up period.

Two cases of meningitis due to Hemophilus influenzae, type B, both in infants, were treated by parenteral and intrathecal streptomycin. One patient received no therapy other than streptomycin. The other had been treated for ten days with sulfadiazine and type-specific rabbit antiserum, but showed little or no clinical response; H. influenzae had persisted in the stained smears of the cerebrospinal fluid. Both patients showed a gradual clinical improvement during streptomycin therapy, and in both cases recovery was complete. Smears and cultures of the spinal fluid were negative for H. influenzae after the first day of streptomycin treatment in both instances.

The fifth case was that of a 4-month-old infant who had a B. proteus infection of a congenital meningocele which failed to respond to penicillin and sulfadiazine. Streptomycin was given intramuscularly and was also injected directly into the meningocele sac. Cultures of the meningocele fluid were negative for B. proteus within twenty-four hours after streptomycin was begun, and remained negative thereafter. Clinical improvement was slow until the seventh day, when the intrathecal injections of streptomycin were ended and sulfadiazine was again given. The fever persisted until the tenth day, when the parenteral streptomycin was stopped. There was no recurrence of infection during the follow-up period.

Comment. In 3 cases of meningitis, 2 of them caused by Ps. aeruginosa and one by H. influenzae, recovery followed treatment with streptomycin alone. In the other 2 patients recovery was probably due to streptomycin, since the other therapeutic agents used had failed to bring about improvement, and infection persisted until the streptomycin was started.

Pulmonary infections

Studies were made on 6 cases of acute or chronic broncho-pulmonary infections caused by gram-negative bacilli and treated with streptomycin. The acute cases included one of bronchopneumonia due to H. influenzae and 2 of pneumonia due to the Friedlander bacillus. One of the latter patients died.

The patient with H. influenzae bronchopneumonia was critically ill when streptomycin was begun, but he showed rapid and progressive clinical improvement during treatment. Two weeks after therapy was ended, he was essentially asymptomatic and x-rays revealed the chest to be completely clear. An abundant and almost pure growth of H. influenzae was obtained from sputum cultures before treatment, but cultures made twenty-four hours after therapy began, and all subsequent cultures failed to show the presence of these organisms.

A patient with pneumonia and bacteremia due to type C Friedlander's bacillus showed rapid improvement after streptomycin was begun. Blood cultures were negative four hours after the initial dose, but sputum cultures were consistently positive for Friedlander's bacilli. The strain recovered from the sputum before treatment was quite sensitive to streptomycin, but the strains recovered on the second day of therapy and thereafter were highly resistant **in vitro** to the action of the antibiotic. This patient's course was protracted; multiple abscesses formed in the consolidated right upper lobe, and although streptomycin was subsequently given by aerosolization and large doses of penicillin were given both intramuscularly and by aerosolization, cough and purulent sputum continued for two months. The abscesses healed slowly, and only fibrotic changes remained in the right upper lobe when the patient was discharged from the hospital.

The third case was one of pneumonia of the right upper and middle lobes due to type A Friedlander's bacillus. Blood cultures in this case were negative. Streptomycin was given after six days of intensive treatment with sulfadiazine and penicillin, during which the patient had grown progressively worse. Considerable clinical improvement followed the institution of streptomycin therapy, and Friedlander's bacilli could not be found in smears or cultures of the sputum after the second day of this treatment. On the fourth day of streptomycin therapy, however, the patient died rather suddenly. A postmortem examination showed consolidation and abscesses of the right upper and middle lobes. Type A Friedlander's bacilli were cultured from the consolidated lung, and these had the same streptomycin sensitivity as the pretreatment strain.

The 3 remaining patients had chronic suppurative bronchiectasis. Sputum cultures in one of them yielded Friedlander's bacillus, type A; in the second A. aerogenes and H. influenzae were present; and in the third, the cultures yielded a heavy and almost pure growth of H. influenzae. Each of these strains was sensitive to less than 10 units of streptomycin. The streptomycin was given by nebulization in all of these cases, and 2 patients received parenteral doses as well.

Two of the patients showed a marked reduction in cough and sputum after streptomycin therapy was started, although small numbers of highly resistant organisms were recovered from cultures of the sputum during and after treatment. The resistant organism in one of the cases was identical with the pretreatment strain, but in the other case a different organism was obtained. The third patient eventually proved to have a bronchogenic carcinoma in addition to a widespread and severe bronchiectasis. That patient showed no clinical response to streptomycin treatment, and sputum cultures continued to yield large numbers of H. influenzae. The organisms recovered from the sputum on the second day of treatment and thereafter were highly resistant to streptomycin, as were those recovered from the lung at autopsy.

Comment. It is not possible to draw final conclusions as to the therapeutic value of streptomycin in gram-negative bronchopulmonary infections, because relatively few cases have been treated with this drug. This small series and the results in similar cases reported by others[9] suggest that some severe cases may respond favorably to streptomycin therapy.

Ear infections

Studies were made on 18 patients who had persistent purulent drainage from one or both ears, and who were treated with local instillations of streptomycin solutions. A

total of 28 suppurating ears were treated: 6 of them were in cases of subsiding acute otitis media, with profuse purulent discharge; 19 resulted from chronic otitis media, and had drained constantly or intermittently over periods of one to twenty-five years; in the remaining 3 ears, the infection was limited to the external canal.

Cultures from 26 of the draining ears yielded gram-negative bacilli, alone or (in 5 instances) mixed with gram-positive organisms. Almost all these organisms were sensitive to streptomycin *in vitro*. Ps. aeruginosa and B. proteus were the strains most frequently isolated. Two of the ears were infected only by staphylococci, and had shown no response to topical instillations of penicillin.

Treatment for the most part was carried out by the patient. It consisted in drying the ear canal and instilling 1 milliliter of a solution containing 1,000 to 20,000 units of streptomycin in saline four times daily. This regimen was continued for one to seven weeks.

In 12 ears, the drainage disappeared during treatment, and did not recur during two to four months of observation. In 13 there was either no response or apparent improvement with a prompt recurrence of drainage after streptomycin was discontinued. In 3 ears the drainage subsided during treatment, but the patients were not followed after treatment. Changes of bacterial flora during treatment and the development of streptomycin resistance were observed frequently in these cases.

Comment. The results in these cases were not uniformly favorable. Nevertheless, it is of interest that simple local instillations did benefit some of these refractory cases. Topical instillation alone probably is not the optimum method of using streptomycin in such cases. Further therapeutic attempts with streptomycin administered both locally and parenterally are indicated. The use of a mildly alkaline solution for the local instillations of streptomycin into the ear canal may possibly serve to enhance the antibiotic activity, and deserves a trial.

Untoward reactions

The reactions observed in this group of cases were similar to those reported by others. The most frequent was pain and tenderness at the site of the injections. In some cases this became quite severe and was associated with the development of large areas of redness and induration. Various combinations of fever, anorexia, headache, malaise, weakness, urticarial rashes, myalgias, and arthralgias were experienced by several of the patients in the latter part of the course of streptomycin therapy. All of these symptoms, however, subsided quite promptly after the injections were stopped.

Histamine-like reactions were encountered by several patients during intravenous injections of streptomycin, and one elderly man had clonic convulsive seizures. These reactions could usually be minimized or avoided by giving the drug in more dilute solution and injecting it more slowly. Several patients also had mild but transient vertigo during treatment, which cleared up when the streptomycin was stopped. In 3 patients an acute labyrinthine disorder, manifested by slight deafness, vertigo, and instability of gait, developed. The condition cleared promptly in 2 cases, but the vertigo and unstable gait persisted in the third patient for more than three months.

The administration of streptomycin by the intrathecal route was accompanied by fever and pleocytosis of the cerebrospinal fluid in 3 cases.

Summary and Conclusions

This small group of cases suggests that streptomycin, at the present time, has an important place in the treatment of certain infections with susceptible organisms. Some infections with gram-negative bacilli that have resisted therapy with other agents have responded favorably to streptomycin. When given in adequate intramuscular doses and together with alkalis by mouth in sufficient amounts to maintain an alkaline urine, streptomycin may arrest the progress of serious destructive infections of the urinary tract and help to preserve the residual renal function. In meningitis due to gram-negative

9. (a) Nichols, D. R., and Herrell, W. E.: Streptomycin: Its Clinical Uses and Limitations, J.A.M.A. 132:200-206 (Sept. 28) 1946. (b) Olsen, A. M.: Streptomycin Aerosol in the Treatment of Chronic Bronchiectasis: Preliminary Report, Proc. Staff Meet., Mayo Clin. 21:53-54 (Feb. 6) 1946. (c) Durant, T. M., Sokalchuk, A. J., Norris, C. M., and Brown, C. L.: Streptomycin Therapy in Hemophilus Influenzae Pulmonary Infections, J.A.M.A. 131:194-196 (May 18) 1946. (d) Learner, N., and Minnich, W. R.: Friedlaender Pneumonia Treated with Streptomycin: Report of a Case with Prompt Recovery, Ann. Int. Med. 25:516-520 (Sept.) 1946. (e) Bishop, C. A., and Rasmussen, P. F.: Klebsiella Pneumonia Treated with Streptomycin, J.A.M.A. 131:821 (July 6) 1946. (f) Committee on Chemotherapeutics and Other Agents, National Research Council: Streptomycin in the Treatment of Infections: A Report of One Thousand Cases, J.A.M.A. 132:4-11 (Sept. 7) and 70-77 (Sept. 14) 1946.

bacilli it may be a life-saving measure when given parenterally and intrathecally. It may also have a place in the treatment of acute and chronic bronchopulmonary infections, and may contribute materially to the management of ear infections, particularly those associated with gram-negative bacilli.

Reactions to streptomycin, except for the labyrinthine disorder, are usually transient, but they are more frequent and more disturbing than those resulting from the use of penicillin. The development of streptomycin resistance in initially susceptible organisms occurs quite frequently during therapy, and limits the usefulness of this antibiotic in many cases.

MORTALITY IN THYROID SURGERY

ROY B. MCKNIGHT, M.D.*

CHARLOTTE

Classification of Cases

In an attempt to classify a large series of goiter cases, certain almost insurmountable difficulties are encountered. The more one tries to correlate the clinical picture with the gross appearance of the excised gland and with its histologic pattern, the more confused he becomes. There is no classification of thyroid disease into which all cases of a large series can be fitted. Neither the Plummer classification nor that advocated by the American Association for the Study of Goiter is entirely satisfactory. There is frequently such overlapping and confusion in the histologic picture that two or more competent pathologists will give conflicting reports which make it impossible to classify the specimen accurately. The clinical picture and the gross appearance of the gland, not to mention the histologic findings, often do not coincide.

It has never been clear to me what is meant by "non-toxic diffuse goiter." Again, why should a "toxic diffuse goiter" (or a diffuse goiter with hyperplasia) be called an exophthalmic goiter when there is not, and never has been, the slightest suggestion of exophthalmos? Nodular or adenomatous goiters constitute a large group with different pathologic entities.

The etiologic factors of goiter, especially hyperthyroidism, are obscure, and it is apparent that hyperthyroidism is not an entity in itself, but is the resultant of various physico-chemical disturbances producing different clinical and pathologic pictures. There must be a "trigger" somewhere which initiates this course of events.

In spite of the difficulties outlined above, I have attempted (table 1) to classify the cases in my series of 1,091 thyroidectomies. I have relied almost entirely on the pathologist's reports, although in a few instances the clinical finding of fulminating hyperplasia is substituted for a pathologic report of *moderate* hyperplasia.

Table 1

Classification	*No. Cases*	*Deaths*	*Per Cent*
Diffuse goiter with hyperplasia	564	1	0.18
with marked or fulminating hyperplasia	160	0	0
with moderate hyperplasia	404	1	0.25
Non-toxic nodular goiter	374	3	0.8
Toxic nodular goiter	116	0	0
Others*	37	1	2.7
Total thyroidectomies	1091	5	0.46

* Including Riedel's thyroiditis, Hashimoto's struma, chronic thyroiditis, simple colloid goiter, abnormally large normal glands, malignancies, and so forth.

Diffuse goiter with hyperplasia

It will be noted that there are 564 cases of diffuse goiter with hyperplasia, 160 of which showed clinically and histologically marked or fulminating hyperplasia—typical Graves' disease. In this subgroup there were no deaths and no semblance of crises; convalescence was generally smooth. These good results are attributed largely to the *intravenous* use of iodine in preparing these patients for operation, and to a reasonably rapid operative technique. The more the gland is manipulated, the less likelihood there is of a smooth convalescence.

In 71.6 per cent, or 404, of the diffuse goiters with hyperplasia, pathologic examination of sections showed moderate hyperplasia. In this subgroup there was one death. The basal metabolic rates in this group varied from minus readings to as high as +60 per cent; they were wholly inconsistent with the microscopic findings, and in many instances with the clinical picture. Many of the thyroid glands in this group were undergoing involution.

Often a patient is referred for surgery with a note reading something like this: "Two months ago she had a definitely toxic goiter. She has been on iodine since and

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seems much improved." In such cases it is difficult to know exactly what one is dealing with. Many borderline cases with definite early hyperplasia present a real problem in diagnosis. Generally speaking, delay is not dangerous in such cases, and if a policy of "watchful waiting" is followed the disease will manifest itself sooner or later. There is no reason to wait for a full-blown Graves' disease to develop, however, before resecting the gland. It would be just about as sensible to tell a patient with acute appendicitis that it has not ruptured yet, so we'll just wait! In such cases I place much reliance on a therapeutic test with iodine. When a patient who is suspected of having an early toxic goiter shows definite improvement after taking organidin in 10-minim doses thrice daily for two weeks, one can be reasonably sure that the diagnosis of early toxic goiter is correct.

Nodular goiter

The nodular goiters include the adenomas: fetal adenomas; cystic, degenerating, hemorrhagic adenomas; colloid inclusions, and so on. Those showing hyperplasia anywhere on microscopic examination are classified as toxic nodular goiters. This classification coincides fairly accurately with the clinical findings of toxicity; however, only a few patients have been in a markedly toxic condition. Very likely we do not see the number of severely toxic nodular goiters in this part of the country that are reported in other sections.

This series of thyroidectomies includes 374 nodular goiters classified as non-toxic, with three deaths, and 116 classified as toxic, with no deaths. No malignancies are included in this group[1].

Too often patients with nodular goiters are told that they do not need surgery because "that little lump is not bothering you; your breathing test is normal." There are at least three reasons why *all* non-toxic nodular goiters should be removed: (1) They are not likely to become smaller, but will almost certainly increase in size; (2) they may become toxic; and (3) about 5 per cent of them undergo malignant change. The operative risk in cases of early, small, non-toxic goiters is practically *nil*.

1. Brenizer, A. G. and McKnight, R. B.: True Adenomas of the Thyroid Gland and Their Relation to Cancer, Tr. Am. Study Goiter, pp. 176-190, 1940.

Other cases

In the remaining group of 37 cases, classified as "others," there was one death—in a patient with Riedel's thyroiditis who died of pulmonary infarction. This small group includes the malignancies, Riedel's strumas, Hashimoto's strumas, simple colloid goiters, and abnormally large normal glands. All these conditions are interesting, but will not be discussed in this presentation. There have been no operative deaths following radical or palliative operations for malignancy[1].

Distribution of Cases According to Race and Sex

When the series is broken down into race and sex (table 2), some interesting facts are revealed.

Table 2

Race and Sex	*No. Cases*	*Deaths*	*Per Cent*
White	1016	2	0.2
Colored	75	3	4.0
White females	925	2	0.22
Colored females	66	3	4.55
White males	91	0	0
Colored males	9	0	0
Total females	991	5	0.5
Total males	100	0	0

There have been no deaths in 100 males and five deaths in 991 females—two in 925 white females (0.22 per cent) and three in 66 Negresses (4.55 per cent). In this series the distribution of the different types of goiters is about the same in both races and in both sexes. No malignancies have been encountered in 75 colored patients. Contrary to reports from other sections of the country, toxic goiter has been no more severe among the colored than among the white patients—in spite of a mortality or 4.0 per cent in the Negroes and 0.2 per cent in the white patients. This difference in mortality is consistent with that reported in other sections and is hard to explain.

Case Histories of the Patients Who Died

The five deaths were the result of (1) bilateral pulmonary infarction, (2) acute hemorrhagic nephritis, (3) unknown cause, (4) pulmonary embolism, and (5) cardiac collapse (?).

Case 1

A 45-year-old white woman with Riedel's thyroiditis did well for two days following resection; then severe respiratory difficulties developed. After consultation, a tracheotomy was done, with no beneficial results. X-ray of the chest showed bilateral

pulmonary infarction. She expired on the fourth postoperative day.

Case 2

A 61-year-old white woman complained of loss of weight, nausea, some pain in the left side, and a non-toxic nodular goiter of many years' duration. The urine showed a trace of albumin and an occasional red cell in the high power field.

Her immediate postoperative reaction was entirely normal, but she did not void. A catheterized specimen showed a scant amount of urine, a 4 plus reaction for albumin, and many red cells. She became irrational, lethargic, and almost anuric; her nonprotein nitrogen rose to 365 mg. per 100 cc. of blood. In spite of excellent and vigorous treatment by the referring physician, she expired on the eighth postoperative day, with the thyroidectomy wound healed. The diagnosis was acute hemorrhagic nephritis.

Case 3

This patient was an obese colored woman of 39 years. She had never been seriously ill, but had had a goiter for more than five years. Examination was negative except for a huge, non-toxic, nodular goiter.

Operation, done under cyclopropane-oxygen-helium anesthesia, was very difficult. Her condition was good throughout the sixty-minute operation, but as the muscles were being closed she suddenly stopped breathing. Artificial respiration was begun and breathing was resumed, only to stop again as closure was completed. She did not have a tracheal collapse, nor was there any recurrent nerve injury. A tracheotomy was done, however, and she was placed under an oxygen tent. The usual supportive medication was administered when she was returned to her bed, but she expired about an hour later. The cause of death is unknown, since autopsy was refused.

Case 4

A colored woman, aged 52, had a definite toxic diffuse goiter when she was first seen. A blowing systolic murmur was heard over the base of the heart. The pulse was 122, the blood pressure 150 systolic, 100 diastolic, and the basal metabolic rate +38 per cent. The struma had recently developed. She responded nicely to organidin in 15-minim doses three times daily, and three weeks later subtotal thyroidectomy was easily performed under cyclopropane-oxygen anesthesia. Her immediate postoperative reaction was uneventful, but she expired suddenly on the second postoperative day with typical clinical signs of pulmonary embolism.

Case 5

A very obese colored woman, 53 years of age, had had a large nodular goiter for twenty-five years. Physical examination was negative except for obesity, a large, non-toxic nodular goiter (measuring 14 by 14 by 7 cm. after resection), and a blowing systolic murmur heard over the entire precordium. The blood pressure was 152 systolic, 84 diastolic.

After a reasonable period of rest in bed, thyroidectomy was easily and rapidly performed with remarkably little bleeding. She was not in good condition after operation and did not regain consciousness during the day. At times her respiration was of the Cheyne-Stokes type. During the first postoperative night she suddenly collapsed; an emergency tracheotomy was done and she was placed under an oxygen tent. This was removed the following morning, when she seemed much better. Her voice was normal, and she took fluids and nourishment freely. For two days she did well and was in excellent spirits.

On the evening of the third postoperative day she had another sudden collapse; she complained only of being extremely hot, and expired within ten minutes. An excellent internist who saw her stated that death was not due to embolism.

Autopsy was not obtained, and the death is listed as cardiac collapse. There were some aspects suggestive of a cerebral accident, and death may have been due to this cause.

Analysis of Mortality Statistics

Most internists and surgeons interested in diseases of the thyroid are familiar with mortality statistics from various reported series over the country at large, and with the higher mortality among Negroes, especially in the South. The very low over-all mortality rate in this series compares favorably with other reports. It has been stated that goiter, especially toxic goiter, is not as severe in some sections as in others. This statement may be true, but in this series there were a number of poor-risk patients —several with "burnt-out goiters" and marked cardiac damage. One woman was admitted in violent crisis, and others have been in an extremely toxic condition.

No ligations have been done in this series, and only two operations have been performed in two stages. The use of intravenous iodine and glucose in the toxic cases rapidly prepares the patients for operation[2]. It is doubtful if any of the deaths could have been avoided with the possible exception of the second death reported.

Factors reducing mortality

(1) *As accurate a clinical diagnosis as possible*, based upon a good history and careful general physical examination, with the necessary laboratory studies. It is very important that the patient's general condition be thoroughly evaluated. All the patients in this series have undergone complete physical examinations, which were correlated with carefully elicited surgical histories and the necessary laboratory studies.

Many reports of this type list and discuss at length basal metabolic findings. Generally speaking, it has been my experience that such findings are of relative value only, and not infrequently are entirely incompatible with the clinical picture and microscopic pathologic anatomy. One basal metabolic

2. McKnight, R. B.: (a) The Use of Intravenous Iodine in Preparing the Patient with Toxic Diffuse Goiter for Operation, North Carolina M. J. 7:590-593 (Nov.) 1946; (b) An Analysis of 1,100 Consecutive Thyroidectomies, South. Surgeon, in press.

reading is just about worthless; several, taken at the proper times by the same technician and with the same machine, may be of distinct relative value, particularly in evaluating progress preliminary to surgery in patients with hyperplastic glands. More significant than a decrease in the metabolic rate, however, is improvement in the clinical picture: slowing of the pulse, decrease in nervous manifestations, possibly some gain in weight, ability to hold the breath longer, and especially a better mental attitude and decreasing apprehensiveness. Hertzler was eternally right when he said, "Don't let a tin can do your thinking for you!" Many patients in this series with non-toxic nodular goiter had been told by other doctors to forget it, since the "breathing test" was normal!

(2) *Proper preparation of the patient for operation.* It may be that the three deaths following operation for non-toxic nodular goiter could have been avoided had more accurate evaluation and treatment of these patients been accomplished preoperatively. The efficacy of iodine in the preoperative preparation of the patient with toxic diffuse goiter is well known; it has reduced a mortality of about 25 per cent to the low rate achieved today. The use of intravenous iodine and glucose in these cases has been reported[2].

The cooperation of a good internist, particularly regarding the use of digitalis and quinidine, is invaluable.

(3) *Proper operative technique.* Each experienced thyroid surgeon has his own method of operating, and this should be adapted to suit the individual case. A reasonably rapid technique, good exposure, adequate hemostasis, and avoidance of such structures as the recurrent laryngeal nerves and the parathyroids, help to lower the mortality and morbidity rates.

(4) *Efficient postoperative care and good nursing.* The services of an alert, intelligent, and sympathetic nurse are indeed invaluable. In many cases, the cooperation of a good internist is essential and frequently life-saving.

The "proper selection of cases" is *not* a factor in reducing the mortality from thyroidectomies, unless the surgeon is one who keeps his operative mortality low by denying the poor-risk patient the benefit of thyroidectomy. Successful operations have been performed in a number of toxic cases with serious cardiovascular complications. It is in such cases, especially in the toxic nodular goiters, that the most brilliant results are frequently obtained. There have been no deaths in this series among patients with very toxic diffuse or toxic nodular goiters. The deaths have been in those cases in which the risk ordinarily would appear to be slight.

Summary

A series of 1,091 thyroidectomies, with an over-all mortality of 0.45 per cent, has been reported. In the 1,016 operations performed on white patients, the mortality was 0.2 per cent. This low rate can be achieved by proper study of the patient, adequate preoperative preparation, a reasonably rapid and careful operative technique, and good postoperative care[3].

3. McKnight, R. B.: Some Observations Drawn from a Series of 500 Consecutive Thyroidectomies, North Carolina M. J. 2:369-372 (Aug.) 1941.

AN OUTLINE FOR DIAGNOSIS AND MODERN TREATMENT OF CENTRAL NERVOUS SYSTEM SYPHILIS

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Considerable interest in the treatment of syphilis was stirred by the discovery in 1943 that penicillin is an effective antisyphilitic agent. Insufficient time has elapsed to establish the degree of effectiveness of the drug in neurosyphilis. However, results from different investigating clinics have been sufficiently comparable to make possible certain guarded recommendations to the profession.

This outline is designed to give the reader a working basis for the separation of cases into clinical groups, and to offer suggestions for treatment. No single treatise of reasonable length can cover the subject adequately, nor give acceptable directions for the treatment of every case. The management of any individual patient is left to the judgment of the therapist. Data to support recommendations herein made are omitted for sake of brevity. In general, the schedules submitted are more conservative than those which have been utilized by the clinics investigating the effects of the drug.

Asymptomatic Neurosyphilis

Some time during the first few weeks after

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the primary syphilitic infection the spirochetes enter the blood stream and are distributed throughout the body, including the central nervous system. In an estimated 40 per cent of untreated cases the organisms remain within the central nervous system. Symptoms and signs resulting from the infection of the central nervous system do not, as a rule, appear for a number of months or years after the original invasion. During the short or long incubation period the disease is labelled *asymptomatic neurosyphilis*, and since no symptoms or signs are present the infection can be detected only by examination of the spinal fluid. Asymptomatic neurosyphilis is therefore the forerunner of any one of the various types of clinical neurosyphilis. Because results of treatment are best during this early phase of the disease, it is important to establish the diagnosis and administer treatment as soon as possible.

Although in any single case of asymptomatic neurosyphilis it is not possible to determine which, if any, of the clinical forms of the disease will ultimately develop, there are several general principles to consider. Symptoms of syphilitic meningitis appear within three to five years, those of chronic meningovascular neurosyphilis within four to eight years, and those of the several types of parenchymal neurosyphilis within five to forty years following the primary lesion. The longer the spirochetes remain within the central nervous system, the greater is the chance of irreparable damage to the nervous tissues and the greater is the difficulty in eradicating the infection. During the asymptomatic period abnormalities of the spinal fluid may be taken as a rough measure of the infection. A strongly positive fluid—that is, one with increased cell count, high total protein, paretic colloidal gold curve, and a Wassermann positive in high dilution—indicates the presence of an active infectious process which may soon lead to symptoms, or it may point to parenchymal disease which has already begun. A weakly positive fluid, although pointing to infection of low grade, gives no assurance that degenerative parenchymal disease will not develop.

Experience has shown that asymptomatic neurosyphilis of short duration responds well to treatment. Poorer results are obtained in cases of longer duration. Primarily because of this difference in prognosis, it is customary to divide the cases clinically into early and late asymptomatic neurosyphilis.

Early asymptomatic neurosyphilis

The diagnosis of early asymptomatic neurosyphilis is made on those cases with one or more abnormalities of the spinal fluid noted within four years after the primary infection. An elevation in cell count or total protein, or both, is sufficient to establish the diagnosis. The Wassermann reaction and the colloidal gold curve may or may not be abnormal.

In early asymptomatic neurosyphilis, invasion of the central nervous system is of relatively recent origin; the organisms have not obtained a firm foothold, and few irreparable changes have occurred. Results of treatment are very good, but caution is needed in giving a prognosis until two years have elapsed following treatment.

Treatment:

1. A total of 3,000,000-4,000,000 units of penicillin, injected intramuscularly in individual doses of 20,000-40,000 units, administered every three hours night and day for seven and a half to fifteen days.

Spinal fluid examinations, including tests for cell count, total protein, colloidal gold, and Wassermann reaction, should be performed every six to eight months until the fluid has been normal for two years. Persistent or recurrent abnormalities in any one of the tests point to inadequate treatment and demand a repetition of the course of penicillin as above described at the end of one year. If this does not serve to reverse the changes and hold the fluid to normal at the end of the second year, fever therapy is indicated.

Late asymptomatic neurosyphilis

This diagnosis is made when the spinal fluid reveals the only evidence of central nervous system infection four years or more after the primary lesion. In cases of this duration, a positive Wassermann reaction is usually obtained, irrespective of the results of the other tests on the spinal fluid. Again, as in the early asymptomatic cases, the degree of the spinal fluid abnormalities is taken as a rough measure of the severity of the syphilitic infection. Because of the longer duration of the infection, it can be assumed that the infectious agent has probably obtained a firm foothold, that it has had ample opportunity to invade parenchymal tissues, and that there is considerable potential danger for the future. Vigorous treatment may be required to eradicate the infection before irreparable damage occurs. The late asymptomatic case is frequently more of a therapeutic problem than early

symptomatic cases, especially acute syphilitic meningitis.

Treatment:

1. A total of 4,000,000-6,000,000 units of penicillin intramuscularly in individual doses of 25,000-50,000 units every three hours night and day for seven and a half to twenty-one days.
2. Bismuth, 0.2 Gm. intramuscularly every three or four days for five doses.
3. Mapharsen, 0.04-0.06 Gm. intravenously every three or four days for ten doses.

The spinal fluid examination should be repeated every six months after treatment. If, at the end of the first six months, a substantial improvement has not occurred—that is, if cell count and total protein have not returned to normal or approximately normal—a repetition of the course of penicillin is indicated. If the spinal fluid shows a relapse or is persistently abnormal in cell count and total protein at any time after the first follow-up at six months, fever therapy should be administered in addition to a second or third course of penicillin. Each case should be followed until the spinal fluid has remained normal for at least two years.

Acute Syphilitic Meningitis

The symptoms of acute syphilitic meningitis appear earlier than those of any other type of neurosyphilis. Symptoms commonly appear before the end of the third year following the initial infection. If symptoms and signs indicative of syphilitic meningitis appear four years or more after the primary lesion, it is assumed that the illness is an acute flare-up of a chronic process, and therefore is more properly classified as chronic syphilitic meningitis.

Acute syphilitic meningitis is characterized by the fairly rapid onset of headache, lethargy, blurring of vision, stiffness of neck, general malaise, and sometimes symptoms pointing to involvement of cranial or spinal nerves, such as diplopia, deafness, tinnitus, or facial paralysis. Physical examination may show a slight elevation of temperature, stiffness of the neck, pupillary disturbances, papilledema, abnormalities of one or more of the cranial nerves, and, rarely, a positive Kernig sign. The spinal fluid is frequently obtained under increased pressure. The cell count is elevated usually to 80 or more cells per cubic millimeter, with a slight to moderate elevation of total protein. The colloidal gold curve is variable and the Wassermann test is positive, except in a few cases in which symptoms appear within a year or so after the primary lesion.

If no treatment is administered, the acute symptoms usually subside in several weeks. Subsequent exacerbations are to be expected however, and after a variable time the clinical and pathologic picture of general paresis or other types of parenchymal disease may appear. Since the meningitis develops early in the course of syphilis, good results are obtained from prompt antisyphilitic treatment. Indeed, relief of symptoms is to be expected within a few days, and complete reversal of the spinal fluid abnormalities may occur in a few months. However, long experience with acute syphilitic meningitis has demonstrated that relapses are likely to occur even years later and that general paresis is the most common form of parenchymal disease to follow. With careful, long-term follow-up, such complications should be avoided.

The results of treatment with penicillin have been very satisfactory in acute syphilitic meningitis.

Treatment:

1. A total of 3,000,000-4,000,000 units of penicillin intramuscularly in individual doses of 20,000-40,000 units, given every three hours night and day for seven and a half to fifteen days.
2. As an added precaution, especially in cases suspected of being chronic, 0.04 to 0.06 Gm. of mapharsen intravenously every three or four days for ten doses immediately following the above course of therapy is recommended.

The spinal fluid should be examined at intervals of four to eight months until two successive normal fluids are obtained; thereafter, every year until the fluid has been normal for five years. A persistently abnormal spinal fluid or a relapse from normal to abnormal after one to one and a half years indicates inadequate treatment and the probability of parenchymal disease. Fever therapy and a repeat course of penicillin are indicated.

Chronic Syphilitic Meningitis
Chronic Meningovascular Neurosyphilis
Late Asymptomatic Neurosyphilis with Pupillary Abnormalities

Within this ill-defined, heterogeneous group are generally placed all cases of neurosyphilis which are of long standing and which exhibit symptoms or signs that do not fit into one of the more well-defined categories. It is assumed that the symptoms and signs in this type of neurosyphilis result from inflammatory changes of the pia-arachnoid membrane, from diseased blood vessels, or from both.

The clinical manifestations in this group are extremely variable. Patients with chronic meningitis may suffer from headache, convulsions, memory defect, or signs of cranial nerve palsies. The spinal fluid usually shows an elevation of the cell count and total protein, and a moderate to strongly positive Wassermann. When the meningitic process is localized over the frontal lobes of

the brain, the clinical picture is indistinguishable from that of general paresis. Other patients may be wholly without symptoms but have abnormalities of the pupils. Still others have one or more episodes pointing to vascular occlusions, and, rarely, the clinical picture of transverse myelitis is presented.

Results of treatment vary greatly. In many cases residual neurologic signs persist even though the disease is arrested; some patients make completely satisfactory recoveries; and others develop general paresis, tabes, and optic atrophy.

Treatment

It is difficult to make general recommendations for treatment of this group. However, because of the potentially grave outcome, the following outline of treatment should be adhered to in each case.

1. A total of 4,000,000-6,000,000 units of penicillin intramuscularly in doses of 25,000-50,000 units every three hours for seven and a half to fifteen days.
2. Bismuth, 0.2 Gm. intramuscularly every three or four days for five doses.
3. Mapharsen, 0.04 to 0.06 Gm. intravenously every three or four days for ten doses.
4. Follow-up as described under the section on acute syphilitic meningitis.
5. Fever therapy six months after treatment, if clinical and spinal fluid improvement has not occurred.

General Paresis

General paresis is the result of spirochetal invasion of the cerebral cortex. The frontal lobes and margins of the sylvian fissures are the areas chiefly affected. If the disease is not arrested by treatment, insanity, convulsions, general paralysis, and death may be expected in the great majority of cases in a period of several years. Symptoms of general paresis may be insidious, with disturbance in judgment, changes in personality, defects in speech, tremors, and forgetfulness; or they may be of rapid onset, with psychotic behavior. The symptoms result from chronic meningitis, vascular disease, and ganglion cell degeneration.

General paresis is the most difficult of all types of neurosyphilis to eradicate. Until the advent of penicillin, all authorities agreed that fever therapy was essential. At the present time some investigators are obtaining sufficiently good results with penicillin *in early cases* to make possible postponement of fever therapy for two or three months to determine the effect of penicillin.

Many factors play a role in determining the outcome, but among the more important factors is the duration of symptoms. If treatment is instituted within the first two or three months, 65 to 75 per cent of the patients may be returned to their previous socio-economic status. If symptoms have been present for six months or more, less than 50 per cent will be restored. Prompt improvement may follow many types of therapy, but relapse is frequent.

When one is treating a paretic patient, it is advisable to have access to a mental hospital. Behavior is unpredictable, and problems in feeding, sleeping, and so forth are common. Furthermore, the psychosis of general paresis may require the same management as comparable psychoses in nonparetic patients.

Treatment:

A. **Early cases** (symptoms less than two months)

1. Penicillin, 6,000,000-10,000,000 units intramuscularly, 40,000-50,000 units per injection, every three hours for fifteen to twenty-one days.
2. Mapharsen, 0.04-0.06 Gm. intravenously every three or four days for ten doses.

If prompt clinical improvement does not occur, or if spinal fluid cell count and total protein have not returned to normal at two to four months after treatment, the patient should have fever therapy.

B. **Late cases** (symptoms more than two months)

1. Fever therapy, preferably malaria.
2. **Concurrently**, 6,000,000-10,000,000 units of penicillin intramuscularly, 40,000-50,000 units per injection, every three hours for fifteen to twenty-one days.
3. Following fever therapy, 0.04-0.06 Gm. of mapharsen intravenously every three or four days for ten doses.

The clinical status and spinal fluid should be followed with great care. Repeat courses of penicillin (although never as beneficial as the first) are often necessary. A second course of fever therapy also may be required, especially if the first course was not malaria. The spinal fluid should be examined every six months, and a gradual reversal of all tests toward normal is to be expected. A majority of cases will require five years for complete reversal. Recurrence of abnormalities in the spinal fluid generally precedes clinical relapse by weeks or months, and indicates the need for more therapy. Because of the tendency of paresis to relapse, it is not safe to discharge patients from follow-up until after the spinal fluid has been normal for several years.

Primary Optic Atrophy

Primary optic atrophy may occur alone or in combination with tabes, general paresis, or both. It most often begins gradually in one or both eyes, and commonly progresses to total blindness within one to three years. When optic atrophy is present alone, it is accompanied by no symptoms other than reduction in vision. Peripheral and central vision are involved. The pathogene-

sis of optic atrophy has not been proved beyond doubt, but it is probably due to an invasion of the cranial portions of the optic nerves by spirochetes. Experience has shown that, even when it is promptly and thoroughly treated, visual loss may continue for a number of months. It is rare for any patient to regain lost visual acuity. The detection and treatment of optic atrophy at the earliest moment are essential if useful vision is to be preserved.

Treatment:

1. Fever therapy, preferably malaria, as soon as diagnosis is made.
2. **Concurrently** 6,000,000-10,000,000 units of penicillin intramuscularly, 40,000-50,000 units per injection every three hours for fifteen to twenty-one days.
3. Follow-up as in general paresis.

Tabes Dorsalis

Tabes dorsalis is a clinical syndrome due to spinal syphilis. Except for the cranial-nerve and pupillary signs, the symptoms of the disease are explained by inflammation and degeneration of the posterior roots of the spinal nerves. Rarely, anterior roots are also involved. In most cases, symptoms begin gradually and progress only slightly over several years; in other cases, however, symptoms may develop rapidly, and control of the legs and the urinary bladder may be lost within a matter of weeks. In some cases, debilitating illness, exhaustion, poor nutrition, and other factors appear to play a contributory role.

Unfortunately, many of the most distressing manifestations of the disease—visceral crises, lightning pains, Charcot joint, and bladder dysfunction—are only slightly affected by antisyphilitic treatment. If treatment is administered early, ataxia may be greatly benefited, but improvement is usually more dependent upon good nutrition and reeducation of muscles than upon antisyphilitic therapy. However, in spite of the fact that many symptoms and signs of tabes are residual and secondary phenomena, the first aim of treatment is to prevent progression by administering antisyphilitic therapy to arrest whatever inflammatory or degenerative process may be present.

The diagnosis of tabes is usually not difficult. The physical examination reveals irregular, unequal pupils which do not react to light, lightning pains, ataxia, positive Romberg sign, loss or reduction in vibration and position sense in the lower extremities, reduced deep-pain sense, atonic bladder, and absent tendon reflexes in the legs. Occasionally, however, when only a few signs are present, it is difficult to establish the diagnosis. Most authorities would accept the diagnosis of tabes in the presence of a positive spinal-fluid Wassermann test if any one of the above listed signs, excluding the pupillary irregularities, are present. The spinal fluid is variable in tabes. In some patients it shows the strong "paretic formula," while others have completely normal fluids ("burnt-out tabes"). More commonly, however, the several tests show slight to moderate abnormalities.

The tabetic patient frequently requires general medical, nutritional, and physical therapy, as well as antisyphilitic treatment. Cases with normal spinal fluid may need no antisyphilitic treatment. Patients with optic atrophy or general paresis should be treated by the methods outlined for those conditions. Fever therapy, which is required in a high percentage of cases, should not be debilitating, lest symptoms and signs of the disease, especially bladder dysfunction, be exaggerated.

Treatment:

1. Penicillin, 6,000,000-10,000,000 units intramuscularly, 40,000-50,000 units per injection, every three hours for fifteen to twenty-one days.
2. Fever therapy two to three months later if **clinical** improvement is not prompt and definite; also if spinal fluid cell count and total protein have not returned to normal six months after penicillin therapy.
3. Spinal fluid should be examined every six to eight months after treatment until it remains negative for two years. A recurrence of abnormal findings in the fluid indicates need for repetition of the course of penicillin.
4. Attention should be directed to nutrition, reeducation of limbs, and bladder function.

Fever Therapy

The usefulness of fever therapy in neurosyphilis has been well established. The exact mechanisms by which it helps to bring about recovery are not known. Since the body temperature cannot be raised safely to the thermal death-point of the spirochetes, however, it may be presumed that the effect of fever is to aid the body's defense against the infection.

Several means of elevating body temperature have been devised. Each method has its proponents, but difference of opinion regarding the relative value of each method is less marked than in former years. All forms of fever therapy carry risk for the patient. Fever therapy should be administered only

in a hospital, and by physicians who have gained experience in its use.

1. *Malaria* is the form of fever therapy most widely used, and there is little doubt that it produces the most satisfactory results. Benign tertian malaria is generally employed, although quartan malaria may be substituted in patients with natural or acquired resistance. In experienced hands, therapeutic malaria carries only slight risk for patients who are physically fit. It is not safe in patients with cardiac, renal, or liver disease and is contraindicated in patients who have had recent pyogenic infections.

2. *Mechanically induced fever* requires special equipment, a well-trained nurse-technician, and a physician experienced in hyperthermy. Although fever induced by this method ranks close to malaria in its therapeutic effectiveness, the above requirements make its use impracticable except in large treatment centers. Because the temperature elevation can be well controlled, and because the fever is not usually debilitating, mechanically induced fever is particularly useful in patients with tabes dorsalis and in other patients with poor nutrition or frail physique.

3. *Protein shock*, by intravenous injection of stock typhoid vaccine, is another widely used method of induction of therapeutic fever. Although it is relatively easy and safe, the results obtained in general paresis and optic atrophy by this method are distinctly inferior to those obtained with malaria and the fever cabinet. In other types of neurosyphilis, the results reported in the literature are more satisfactory.

Conclusions

A brief outline of the development, clinical picture, and treatment of the several types of neurosyphilis is presented. Case reports, statistics, and other details are omitted. Some of the recent original articles are appended for reference[1-9].

1. Penicillin is a potent therapeutic agent in all forms of neurosyphilis. It is of value only when activity of the syphilitic disease is present. The spinal fluid is the best guide to activity.

2. Cases of neurosyphilis treated with penicillin require careful clinical and spinal-fluid follow-up for many years in order to detect evidence of a possible relapse. Repeated courses of treatment are often necessary.

3. Cases of late asymptomatic and parenchymal neurosyphilis which do not show progressive improvement in the spinal-fluid abnormalities should have fever therapy.

4. Patients with optic atrophy or general paresis who have had symptoms for two months or more should have fever therapy, preferably malaria, and penicillin simultaneously as soon as the diagnosis is established.

References

1. Moore, J. E., and Mohr, C. F.: Penicillin in the Treatment of Neurosyphilis; Asymptomatic Neurosyphilis, Am. J. Syph., Gonor. & Ven. Dis. 30:405-419 (Sept.) 1946.
2. Hahn, R. D., and Clark, E. G.: Asymptomatic Neurosyphilis: Prognosis. Am. J. Syph., Gonor. and Ven Dis. 30:513-548 (Nov.) 1946.
3. Nelson, R. A., and Moore, J. E.: Acute Syphilitic Meningitis Treated with Penicillin, Am. J. Syph., Gonor. and Ven. Dis. 30:227-230 (May) 1946.
4. O'Leary, Paul A., and Kierland, Robert R., Today's Treatment of Syphilis, J.A.M.A., 132:430-434 (Oct. 26) 1946.
5. Callaway, J. L., et al.: The Use of Penicillin in the Treatment of Syphilis of the Central Nervous System; Report of 100 Patients, Am. J. Syph., Gonor. and Ven. Dis. 30: 110-124 (Mar.) 1946.
6. Gammon, G. D., et al.: Penicillin Therapy Alone in Neurosyphilis: An Analysis of Clinical Results, Ann. Int. Med. 25:412-432 (Sept.) 1946.
7. Reynolds, F. W., Mohr, C. F., and Moore, J. E.: Penicillin in Treatment of Neurosyphilis; Dementia Paralytica, J.A.M.A. 131:1255-60 (Aug. 17) 1946.
8. Rose, A. S. and Solomon, H. C.: Penicillin in the Treatment of Neurosyphilis; Study of 100 Cases Followed Twelve Months or More, J.A.M.A. 133:5-10 (Jan. 4) 1947.
9. Koteen, H., Doty, E. J., Webster, B., and McDermott, W.: Penicillin Therapy in Neurosyphilis, Am. J. Syph., Gonor. and Ven. Dis. 31:1-13 (Jan.) 1947.

THE PSYCHIATRIC ASPECTS OF GYNECOLOGY AND OBSTETRICS

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In medical education today, increased emphasis is being placed upon the teaching of psychiatry. The prevention, early recognition, and intensive treatment of the more serious mental reactions are stressed. Of more practical significance to the man preparing for general practice or for one of the non-psychiatric specialties is the acquisition of the psychiatric point of view in the treatment of all patients. The evolution of this role of psychiatry in medical education and practice is definitely associated with, if not the result of, the great success of modern scientific methods in medicine.

Advances in Scientific Knowledge Responsible for Neglect of the Emotional Factor

During the past seventy-five years, mankind in western civilization has reached a

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high level of physical health, largely as a result of these methods. We are apt to take modern standards of health for granted, but they are maintained through a constant application of our knowledge of disease and its prevention. This application of knowledge is illustrated in the sanitary measures safeguarding our food and water supplies, and in the immunizing procedures protecting us all from diseases which often proved fatal in former centuries. Our many technical devices and methods in diagnosis have enabled us to achieve a high degree of precision in the application of preventive and curative measures. The discovery of microscopic organisms as the cause of disease transformed the practice of medicine. This knowledge, followed by the application of antisepsis, asepsis and other technical improvements, made possible surgery as we know it today. The development of powerful and specific drugs also has done much to combat disease. We are familiar with the advances which these scientific contributions have made possible in the fields of obstetrics and gynecology.

It is not surprising that while the medical man was learning and mastering this great body of scientific knowledge, his attention was turned from the patient as a person. This statement was certainly never true of all physicians, even those most skillful in technical procedures. The gynecologic and obstetric patient, furthermore, has a way of demanding this consideration of herself as a person, even from those with little innate ability or training in the psychiatric point of view. In the days before the dawn of modern scientific medicine, however, the physician had to depend more upon his understanding of the patient's family background and temperament, her whims, personal peculiarities, and idiosyncracies. This is an approach as old as the first wise physicians. Certainly the position of the old family doctor afforded an excellent opportunity for the development of this point of view. Often his good results were based largely upon his thorough knowledge of the patient's personality and his ability to teach her and influence her through suggestion, reassurance, and persuasion.

In presenting the psychiatric aspects of gynecology and obstetrics, I do not wish to minimize the importance of all the praiseworthy technical advances in the specialties. They are standards which must be maintained, improved, and refined by the trained workers in the field. I do wish, however, to emphasize the role of the emotions and the importance of taking into consideration the psychologic make-up of individual patients.

Psychiatric Factors in Gynecologic Disorders

Dysmenorrhea

In eliciting personal histories and personality development from our patients with mild or serious psychiatric disorders, psychiatrists encounter many distorted ideas associated with the beginning of menstruation. The phenomenon is interpreted by some as an injury. Others believe they are suffering from a serious disease, which they interpret as a punishment, while others react with feelings of shame or disgust. Frequently these attitudes are found in patients who complain of dysmenorrhea. When the organic factors have been ruled out by careful gynecologic examination, we should investigate the psychologic and emotional aspects of the problem. In addition to misinterpreting the phenomenon originally as being due to injury or disease, such girls are apt to reject their feminine role.

In a study of 50 women patients who were addicted to alcohol, we found that 40 of them suffered from dysmenorrhea. Most of them had had previous medical treatments, including glandular therapy, but the symptoms had persisted. Our gynecologic consultant found no organic basis for the complaint. Our psychologic studies did reveal that these women repudiated their femininity. Menstruation was disgusting to them, and had been interpreted as an insult or injury to a self-centered or narcissistic type of personality, one aspect of a faulty adjustment to marriage and motherhood. The presence of actual organic disease does not preclude the presence of emotional and psychologic difficulties, and if the patient with gynecologic complaints is given the opportunity to unburden, many distorted notions can be corrected and the patient can be taught what is the normal or average wholesome attitude about this physiologic phenomenon.

Frigidity and dyspareunia

The problems of frigidity and dyspareunia, when organic factors are ruled out, are usually a part of a complex neurosis which requires psychiatric treatment. The

psychic representations of the generative organs, together with emotionally toned misconceptions and strivings in the development of the individual, have a structure or psychopathology which is more complex than the anatomy, physiology, and pathology with which the gynecologist is familiar. In undergraduate and graduate medical education, we are attempting to teach this concept. In practice today the neurotic complaints of frigidity and other such serious maladjustments require the cooperation of the gynecologist and the psychiatrist for the best results in treatment.

The menopausal syndrome

The menopause is the period of a woman's life when we see a significant correlation of physiologic and psychologic factors. Most medical men are familiar with the dramatic physical changes—the cessation of menses, the loss of the power to conceive, and the associated glandular changes. Of greater importance are the psychologic forces at work in women who have trouble at this time. We are aware of the many serious physical diseases such as carcinoma and hypertension which occur during these decades. Careful physical examinations at intervals, and medical and surgical treatment if indicated are unquestionably recommended, but we must be familiar with the psychologic aspects of this epoch to be of service to our patients. The woman feels that she is not needed by her children and family; there is a tendency to be hypochondriacal; and there are preoccupations with death. With a loss of physical beauty, there are feelings of neglect and jealousy. Sometimes increased erotic drives may bewilder and embarrass the patient. Worries over finances may be indicative of her general feeling of insecurity. An investigation of such personality factors should accompany the regular physical examinations.

The physician as a sympathetic listener can be of great assistance in the act of the patient's unburdening. He can then teach the woman in simple and understandable language what is going on. The successful adjustment involves a graceful changing of attitudes and the adopting of new interests in the home and in the community. The patient must realize that the adjusted woman after the menopause must be different from what she was before. She must learn to grow old gracefully and change her interests and attitudes, so that she feels that her life is useful to the community as well as to her family, who have grown and changed. A little guidance in this sphere of a woman's life is fully as helpful as sedative and endocrine preparations.

Psychiatric Factors in Obstetrics

It is beyond the scope of this paper to take up in detail the serious psychiatric disorders associated with pregnancy and childbirth. It should be stressed, however, that except for the acute delirious reactions on a toxic or infectious basis, the mental manifestations are no longer spoken of as postpartum psychoses, but are classified according to the symptoms. We speak of a manic-depressive, schizophrenic, or neurotic reaction which is precipitated by childbirth. The mental illness is an expression of the personality and the constitution which is attempting to adjust to this life situation. This tragic complication is not very common, occurring about once in every thousand births. Such patients require treatment in mental hospitals.

In the specialty of obstetrics, we are impressed with the great progress which has been made and the praiseworthy refinements in technique. The prenatal care, the management of labor, and the postpartum care of the mother and baby approach perfection in many of our hospitals. At the same time, the woman may be neglected as far as her personality and emotional reactions are concerned. The patient as a person may be wrought up and tense, and burdened with many distorted notions about what she is going through. She may receive much advice and many suggestions from relatives and friends, who only increase her fear and anxiety. There is no subject, unless it be death, that is surrounded by more superstitions and false beliefs.

In considering the psychologic aspect, I do not mean to imply that the attention to the patient's physical well-being is to be minimized. I do recommend, however, that more attention be given to the patient as a person. It has been said that the obstetrician should be the ideal person to practice mental hygiene. He sees the patient at an important period in her own life: the time of the launching of a new one. During the prenatal period, the woman has the opportunity to unburden many distorted notions and beliefs and can receive through simple teach-

ing correct and constructive attitudes. In this way a great deal of needless suffering and tension can be relieved. The calm and poise of the mother have a far-reaching effect upon the mental health of her child and of the family group.

Pregnancy

We are familiar with many of the personality changes which occur in the average woman during pregnancy. In some we see an exaggeration of unpleasant traits. The husband should know about this, and be taught to have an understanding and tolerant attitude. On the other hand, the normal joy and exuberance of some young mothers may be irritating to the young husband who is beginning to feel the pressure of increased responsibilities, especially when the wife gives him the feeling that she is now definitely outdoing him in this new accomplishment. The matter of sex relations should be discussed with both husband and patient. Needless conflict and friction are caused by not facing this problem squarely and with common sense.

The psychologic aspects of the nausea and vomiting of early pregnancy, when all physical causes have been ruled out, are worthy of our attention. Nausea is frequently an expression of uneasiness in adjusting to something new—a denture or a new pair of shoes, for example. We must remember that a person can be of two minds about one thing at the same time. Women of deep maternal feeling and disposition may entertain contrasting feelings, or ambivalence, as it is called, in regard to pregnancy. Their casual or accidental remarks and dreams may show a rejection, even though consciously they may want a baby. Nausea and vomiting may express this rejection. Our language graphically portrays the emotional value of the individual's antipathy to any idea or state, when we say that she cannot swallow or stomach a certain thing. A discussion of such concepts by the obstetrician with the pregnant woman, together with positive and constructive suggestions, has proven helpful.

Among intelligent girls we frequently meet with the misconception that kissing causes pregnancy and that babies are born through the rectum. Even today certain primitive people believe that sexual intercourse has nothing to do with impregnation. They believe that seeds from certain plants must be eaten to produce offspring. We also know that many people can "stomach" or "swallow" risque stories about the gastrointestinal tract and its functions, but will wince at any story about the genitals or their functions. Such emotionally toned attitudes may be at the basis of the gastrointestinal tract's expression of emotional conflict when the individual is in the early stages of pregnancy.

Labor

Today we meet a great many young women who have achieved success in business or professional careers prior to marriage and childbirth, and who are resentful of having to devote most of their drives and energies to the domestic adjustment, or who think the maternal career is of minor importance and can be naturally and easily pursued in an offhand way without fully committing themselves to the undertaking. It is among such women that we find mothers who are poorly prepared psychologically and emotionally for the adjustment demanded by childbirth. Some women think that childbearing will cause irreparable damage to their physical beauty, or that all sex attraction and drive will be lost. Dr. Frederick W. Dershimer[1] has shown that such mental attitudes have a marked influence on the length of labor—but of more importance for the present argument is the fact that the patient can be given a point of view vital to her present and future mental health.

The postpartum period

It is well for those who are around the young mother after delivery to take into consideration the effect of exhaustion on the mother's first response to her baby. In many instances there is a lack of interest or rejection at first. This may be due to a low level of energy. A more common-sense explanation for a young mother's lack of enthusiasm for her baby may be that she has not had time, or is not given time to become acquainted with her child as a person, and most of her attention is centered on her own pride of achievement in production. Under these circumstances a casual word or look of disapproval is enough to stir up needless guilt. In our well organized hospitals, we have to a great extent neglected the mother-child relationship. Nurses are forced to put schedules and routines ahead of the

1. Dershimer, F. W.: The Influence of Mental Attitudes in Childbearing, Am. J. Obst. & Gynec. 31:444-454 (March) 1936.

mother's desire to get to know her baby, and in many hospitals, if the mother is not nursing her child, she may see it only once a day. For the rest of the time she is pampered with presents and flowers and has no opportunity to realize her real function. Then comes the sudden descent to all the realities of home adjustment, which can be catastrophic for many mothers unless adequate help is available. We should give more thought to establishing the mother-child relationship while they are still in the hospital. Trained help at home for a few weeks is also most important, and I have always recommended this for women who have had previous mental disorders.

Conclusion

The maternal state has something more than its anatomic, physiologic, pathologic and surgical aspects. There is a psychologic structure in the personality of the woman who is passing through this biologic experience which may fit in naturally and harmoniously with what is actually occurring, but which may also be distorted and poorly organized. If this state can be corrected or ameliorated, we are administering psychotherapy of long lasting value to the family and to society.

LOCATING THE APPENDIX

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The appendix may be located anywhere inside or outside the abdominal cavity that it can reach. The deciding factors involved are:

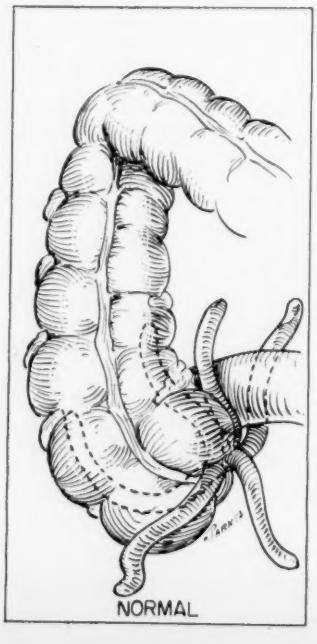
1. **Opportunity for egress from the abdominal cavity.**
2. **Position of cecum as affected by embryologic development.**
3. **Presentation of cecum as affected by rotation.**
4. **Mobility of cecum.**
5. **Peritoneal relations of cecum and appendix.**
6. **Length of meso-appendix.**
7. **Length of appendix.**
8. **Direction in which appendix lies.**
9. **Situs inversus.**
10. **The constant relationship that the appendix bears to the longitudinal bands of the cecum and to the ileo-cecal junction.**

The tenth factor listed above constitutes the salvation of the patient and surgeon. It is the constant in a long list of variables. An appreciation of this factor and a knowledge of the variables provide the surgeon with a simple and confident approach to his problem when the appendix is hard to find.

Possible Positions of the Appendix

Having recognized the fact that the first nine factors in the above list allow a wide range, we realize that the appendix may be practically anywhere in the abdomen, in the fossae, pouches, and canals thereabouts, or in any region with which the abdomen may normally or by anomaly or pathologic process communicate. Thus, in the case of a ruptured diaphragm or a congenital diaphragmatic hernia, the appendix may be entirely inside the thoracic cavity. It may be in the scrotum in an inguinal hernia, or in the thigh in a femoral sac. As a matter of fact, if the hernia is a sliding one of the cecum, the appendix may be in the scrotum or thigh outside the sac. It is frequently outside the peritoneal cavity in the abdomen, lying behind the colon, across the kidney, over the ureter, or back of the duodenum and pancreas. Not infrequently it is located retroperitoneally behind the terminal ileum.

An appendix 10 inches long, starting at any place that the cecum may be located and proceeding in any direction from its base, can really go places. A fine knowledge of anatomy and an excellent technique may be necessary to dissect it out without injuring important structures. Incidentally, the interpretation of symptoms and physical findings in persons with such appendices acutely inflamed may present difficult problems.



1. Conventional drawing, showing the locations and relations of the appendix.

* Chief, Surgical Service, Alamance General Hospital; University of North Carolina Medical School, 1918.

Location of the Normally Placed Appendix (Fig. 1)

If the surgeon is operating through the usual McBurney incision, he will, in a large percentage of cases, find the appendix quite easily with his trained fingers, or else will recognize the cecum by its relatively white color contrasted to the pink or more variable color of the adjacent coils of small intestines. When a fairly mobile cecum is lifted up, some part of the appendix usually appears. If the appendix is acutely inflamed and is bound in with an inflammatory mass, the whole of which is stuck together and covered with lymph and fibrinous exudate, the problem then is one of recognizing cleavage planes and separating them. That is a problem of technique and is outside the scope of this paper. We are concerned with discussing a method for determining the anatomic location of the appendix.

Location of the Abnormally Placed Appendix

If the appendix is difficult to locate, it is wise to cease hunting directly for it, enlarge the incision adequately, and proceed on the basis of item 10 of the foregoing list. An attempt is first made to identify the junction of the small and large gut. This identification in itself may be difficult, but the ileo-cecal junction is the basic anatomic landmark. If it is hidden high behind the cecum, however, the surgeon will follow the ileum as far as he can and then project in his mind the probable point of junction. The appendix is found by following one of the longitudinal bands of the large gut to the base of the appendix. The longitudinal bands run from the appendix to the rectum. The importance of identifying the ileo-cecal junction lies in the fact that, in the presence of anomalies, it is frequently difficult to be sure in which direction to proceed along the longitudinal band. If one knows where the ileo-cecal junction is, he knows which way to go and approximately how far.

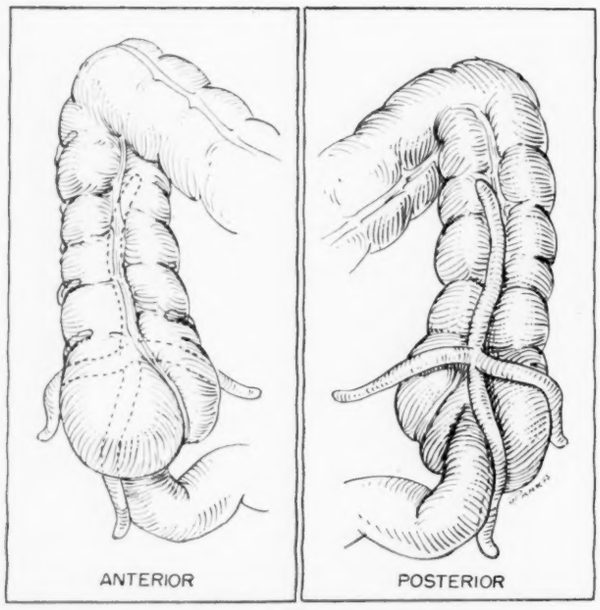
A useful analogy

The relationship of terminal ileum, cecum, ascending colon, longitudinal band, and appendix is well illustrated by the components of the right hand and forearm (fig. 2). The thumb represents the terminal ileum. The wrist and forearm represent the ascending colon. The hand with middle, ring and little fingers closed represents the cecum. The extensor tendon to the index finger represents a longitudinal band on the cecum, and the index finger represents the appendix. These relations, in our experience, are constant for hand or gut. The relative positions remain the same, regardless of contortions.

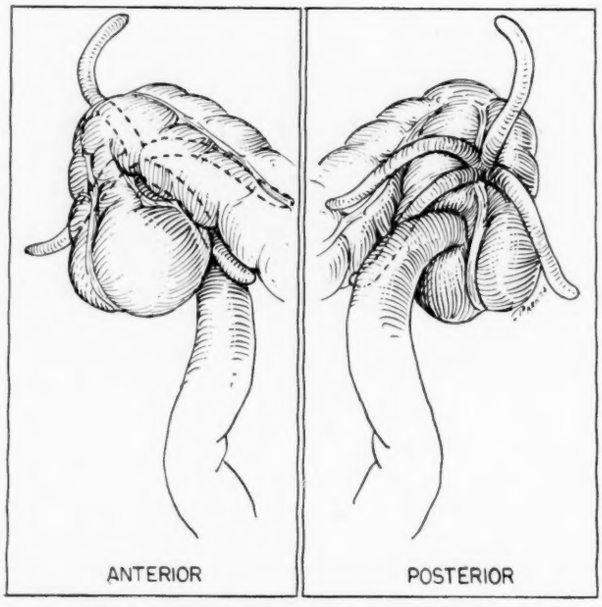
2. Photograph of right hand, with extensor tendon to index finger inked in to represent longitudinal band on cecum. Thumb is analogous to ileum, hand to cecum, wrist to ascending colon, and index finger to appendix.

In this comparison, if the index finger were to assume all the possible positions of the appendix, it would have to be attached to the hand by a universal joint, so that in addition to being extended and folded into the palm it could also be moved behind the thumb, along the ulnar side of the hand, and over the dorsum of the hand. Furthermore, supination and pronation of the hand would have to allow 360 degrees of motion in order for the thumb to simulate all the positions of the terminal ileum in that plane, for the ileum may enter the cecum from front, back, or either side (fig. 3, 4, and 5). To get to the lateral side it may cross the cecum in front or behind. Flexion and hyperextension of the wrist also serve to illustrate other relationships of the cecum and ascending colon to the ileo-cecal junction and appendix. If the hand were boneless, the similarities would be greater.

The peritoneal relationships of the appendix in this analogy to the hand can be



3. Anterior and posterior views, showing locations of the appendix when the terminal ileum enters the cecum from below and behind.



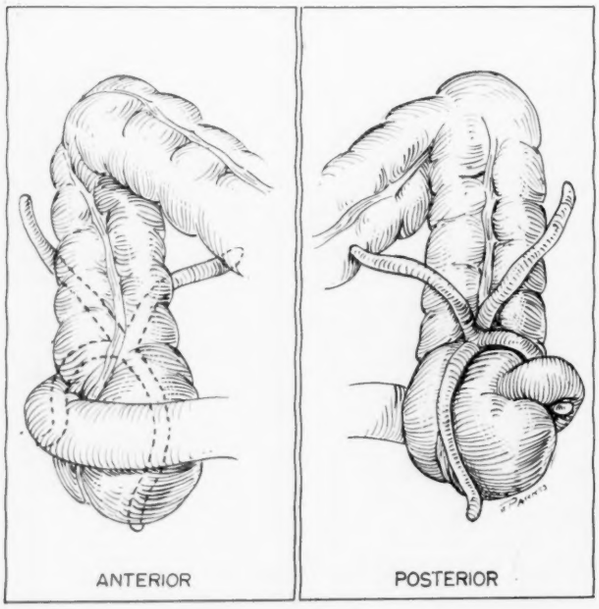
5. Anterior and posterior views, showing location of appendix in right upper quadrant when the terminal ileum enters the cecum from behind. In this condition there frequently is no descending colon.

illustrated by using a handkerchief to represent the peritoneum and spreading the handkerchief so as to cover more or less completely the wrist, hand, thumb, and index finger, allowing only some provision for the entrance of a blood supply. Any degree of coverage used will find a counterpart in the abdomen, as regards the relationship of terminal ileum, cecum, and appendix to the peritoneum.

In this visual comparison of hand to gut we find these anatomic parts holding similar constant relations:

Right Hand
Thumb = Ileum
Wrist = Ascending Colon
Hand (with middle, ring and little fingers closed against palm) = Cecum
Extensor tendon to index finger = Longitudinal band
Index finger = Appendix

The simple conception outlined above often helps to locate the appendix and to be sure of its relationships. The surgeon just places his right hand in a position as nearly like that in the abdomen as he can, then by analogy deduces the location of the appendix.



4. Anterior and posterior views, showing location of appendix when the terminal ileum crosses in front of the cecum to enter it from the lateral side.

Discovery of a new germ-killing agent, isolated from California Spanish Moss, has been announced by the U. S. Public Health Service. The crystalline substance, newest on the long list of materials tested for disease-destroying properties, appears to have an inhibiting effect on the process of tuberculosis in guinea pigs, according to Dr. Alfred Marshak of the Tuberculosis Control Division. The effect of the agent on the progress of tuberculous disease in humans has not been determined since no human testing has been done.

The agent was isolated and the subsequent experimentation conducted by the Division's Field Studies Section at the Hopkins Marine Station and the Rockefeller Institute for Medical Research.

California Spanish Moss, a lichen technically known as **Ramalina reticulata,** grows on the west coast of North America from California to Alaska. —NCTA News Letter, April, 1947.

Veterans filing applications for hospital or domiciliary care continue to total around 70,000 monthly, Veterans Administration said.

SOME CONTRIBUTIONS TO PERIPHERAL VASCULAR PHYSIOLOGY AND THEIR THERAPEUTIC IMPLICATIONS

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Rational therapy of any disease depends upon a thorough knowledge of the physiology of the systems involved. Such a knowledge not only enables the therapist to institute procedures that tend to restore normal function, but also prevents him from inadvertently employing measures that might augment some of the disturbances already present. Of no other field is this statement more true than of peripheral vascular disease, where the use or abuse of relatively simple therapeutic methods may determine the survival of limbs and even of life itself. For this reason, and also because of the increasing incidence of peripheral vascular disease in our aging population, it has seemed worth while to measure with accuracy the circulatory effects of various therapeutic procedures that have been or might be used in the treatment of peripheral vascular disease. The following is a partial account of these studies, which are still in progress.

The Effects of Venous Occlusion

Largely because of a misinterpretation of earlier physiologic studies on reactive hyperemia[1], the method of intermittent venous occlusion was devised for the treatment of peripheral ischemia, on the theory that it would cause the blood flow to be increased through the areas where the venous pressure was elevated[2]. The fallacy of this concept has been proved by the results of four different methods of study on human extremities[3].

When a blood pressure cuff placed proximally on a limb was inflated to pressures greater than the venous pressure but less than the diastolic, the following effects were noted: (a) the velocity of blood flow distally through the cutaneous capillaries was observed microscopically to be decreased, (b) the temperature of the digits was found to be reduced as compared with that of the opposite control limb, (c) the blood flow measured plethysmographically in an entire segment of the limb was decreased, and (d) the arterio-venous oxygen difference of the blood in the limb was increased. There were no signs of an increase in the circulation during inflation of the cuff; on the contrary, there was every indication of a decrease.

It is true that for a short period *after release* of the venous congestion in normal subjects the blood flow, as measured plethysmographically, was slightly increased. This reactive hyperemia after release of the compression was perhaps one of the best evidences that a decrease in blood flow had occurred during the previous congestion. However, like the reactive hyperemia which occurs after release of an arterial occlusion, it apparently did not repay the debt incurred during the previous obstruction of the circulation. Moreover, as others[4] have demonstrated, in limbs with continuous, severe ischemia the mechanism of reactive hyperemia already is operating maximally and cannot be increased by further reduction of the blood flow.

Therapeutic implications

These results indicate that continuous or intermittent occlusion of the venous circulation in a limb by inflation of a blood pressure cuff to pressures greater than venous, but less than arterial, does not increase the blood flow distally, but, on the contrary, decreases it. Since in severely ischemic limbs an increase in blood flow appears to be the primary therapeutic need, the use of any procedure that would increase ischemia, even intermittently, seems contraindicated. It cannot be denied that intermittent venous occlusion might promote lymphatic drainage or produce some other desirable physiologic effect. It seems doubtful, however, that such possible beneficial effects could outweigh the ill effects of further ischemia.

The Effects of Arterial Compression

Studies with cuffs on the limbs were then extended to include observations of the circulatory effects of pressures greater than

From the Evans Memorial and Massachusetts Memorial Hospitals and the Boston University School of Medicine.

* University of North Carolina Medical School, 1931.

1. Lewis, T., and Grant, R.: Reactive Hyperaemia in Man, Heart 12:73-120 (June) 1925.
2. (a) Collens, W. S., and Wilensky, N. D.: Intermittent Venous Occlusion in the Treatment of Peripheral Vascular Disease, J.A.M.A. 109:2125-2130 (Dec. 25) 1937.
   (b) Linton, R. R., Morrison, P. J., Ulfelder, H., and Libby, A. L.: Therapeutic Venous Occlusion, Am. Heart J. 21:721-742 (June) 1941.
3. Friedland, C. K., Hunt, J. S., and Wilkins, R. W.: Effects of Changes in Venous Pressure upon Blood Flow in the Limbs, Am. Heart J. 25:631-647 (May) 1943.
4. Landowne, M., and Katz, L. N.: Dynamics of Blood Flow in Thrombo-Angiitis Obliterans, Proc. Am. Soc. Clin. Investigation, J. Clin. Investigation 20:460 (July) 1941.

diastolic, but less than systolic arterial pressure[5]. When proper pressures (selected by trial and error) were used in such cuffs placed proximally on a limb, the arterial pressure recorded distally through a needle connected to a Hamilton manometer was found to exhibit a most remarkable reaction. There was an immediate *increase* in the distally recorded diastolic pressure, resulting in a sizable elevation of the distal mean arterial pressure. The distal venous pressure rose immediately in the same way as when subdiastolic pressures were used in the cuff, except that the rate at which it rose *increased in proportion to the height of the distal mean arterial pressure.* However, when too-high cuff pressures were used, there was an immediate lowering of the distally recorded systolic, diastolic and mean arterial pressures, and the distal venous pressure rose more slowly.

Only with a limited range of cuff pressures was there an immediate increase in effective arterial pressure distally. Within this range, blood flow recorded plethysmographically was found to be definitely greater than that obtainable with any subdiastolic pressure in the cuff. However, it is important to point out that such increases in blood flow were only of brief duration, because the associated rise in venous pressure was great enough to impede blood flow in the manner described above. Moreover, unless exactly the right cuff pressures were used, the distal arterial pressure and blood flow were decreased rather than augmented.

The proper cuff pressures could not be selected in advance, but had to be determined by trial and error while the distal arterial pressure or blood flow was actually being recorded. Not only was the range of favorable cuff pressure usually narrow, but it varied markedly in different individuals and even in the same limb under different conditions. The range was wider when the blood flow distally was severely reduced prior to the experiments, or when the systemic arterial pulse pressure was large. These considerations and other collateral observations led to the conclusion that the mechanism by which this method enhanced the diastolic arterial pressure was a reduction of the regurgitant or retrograde flow that has been shown to occur in peripheral arteries during diastole[6]. The cuff evidently acted as a peripheral valve to prevent the backward movement of blood in the artery whenever pressure in the artery fell below the pressure in the cuff. The retention of this additional volume of blood in the distal arterial segment increased the pressure within it and the outflow distally from it.

Therapeutic implications

These results demonstrate that intermittent arterial compression by means of a proximal cuff inflated to exactly the right pressures can cause an increase in blood flow distally. The correct range of pressure is narrow and unpredictable, but is wider when there is a large pulse pressure or a markedly reduced peripheral blood flow (with considerable retrograde arterial flow during diastole), or both. Thus a beneficial effect on blood flow would be more likely to occur (with *any* supradiastolic but subsystolic cuff pressure) in just those patients most in need of it—namely, those with generalized arteriosclerosis associated with peripheral ischemia and a wide arterial pulse pressure. This mechanism might be the explanation of some of the good results reported to have followed intermittent inflation of cuffs on ischemic limbs.

For general use as a practical method of therapy, however, the value of this procedure seems doubtful. In the first place, one can never be sure he is increasing arterial pressure and flow distally unless he is actually measuring them. Therefore, he has no way of selecting either the pressure or the time intervals at which the cuff should be inflated. Furthermore, there is a possibility of decreasing the flow distally, a certainty of decreasing it locally[7], and a probability of traumatizing the tissues, and especially the veins, directly beneath the cuff. For these reasons the method would appear to be of little value in the routine treatment of peripheral vascular disease.

The Effect of Local Compression

Careful measurements of skin temperature, plethysmographic blood flow, and ar-

5. Wilkins, R. W., and Bradley, S. E.: Changes in Arterial and Venous Blood Pressure and Flow Distal to a Cuff Inflated on the Human Arm, Am. J. Physiol. 147:260-269 (Oct.) 1946.

6. (a) Gregg, D. E., et al.: Observations on the Accuracy of the Thermostrohmuhr, Am. J. Physiol. 136:250-262 (April) 1942.
   (b) Shipley, R. E., Gregg, D. E., and Schroeder, E. F.: An Experimental Study of Flow Patterns in Various Arteries, Am. J. Physiol. 138:718-730 (April) 1943.

7. Halperin, M. H., Friedland, C. K., and Wilkins, R. W.: The Effects of Local Compression upon Blood Flow in the Extremities of Man, in press.

terio-venous oxygen difference in limbs, before, during, and after local application of pressures ranging from 10 to 60 mm. of mercury, have consistently shown blood flow to be reduced proportionately to the pressure used[7]. Even mild local compression (10 to 20 mm. of mercury) definitely restricted blood flow, and reactive vasodilatation, if present, was not compensatory either during the compression or after its release.

Part of the reduction in flow undoubtedly was due to the immediate increase in local venous pressure and the associated decrease in the arterio-venous pressure gradient. Possibly part of the reduction was due to the decrease in caliber of the compressed vessels and the resultant increase in frictional resistance. In any case, the reduction of blood flow occurred immediately, and persisted with no evidence of even a temporary augmentation locally during compression. After release there was a short period of reactive hyperemia, which appeared to be related more to the degree of the previous compression than to its duration.

Therapeutic implications

These results clearly show the detrimental effects of even small increments in local pressure upon blood flow in normal limbs. Presumably in limbs with ischemic vascular disease these effects are greater. The implications are obvious that compression severely restricts the circulation locally. This should be borne in mind when bandages, splints, casts, elastic stockings, or even light coverings are applied to the limbs of patients suffering from peripheral vascular disease. Everyone treating such patients has observed the detrimental effects produced by the pressure even of the bedclothes upon the body prominences. The weight of the patient himself obviously is most important, and is the direct cause of decubitus ulcers. Every effort should be made therefore to avoid, or at least intermittently to relieve, these types of compression. The patient himself must be taught the dire consequences of local pressure, especially those of tight shoes, stockings, bandages, dressings, and corns or bunions, upon ischemic feet. Probably no other mechanical factor is as important in the management of these patients as the avoidance of areas of pressure.

The Effect of Elevation and Dependency

Elevation of the limbs above the heart level decreases blood flow through them whereas dependency increases the flow[8]. Despite this well established fact, many clinicians continue to advocate elevation and to advise against dependency of the limbs of patients with peripheral ischemia. Most such patients, if left to their own devices, will place their ischemic limbs in a dependent position, the only ill effects of which appear to be local dilatation of the veins and the accumulation of edema fluid. Even these undesirable effects can be avoided by moving the limbs alternately from a dependent to a horizontal position.

Observations of skin temperature of the extremities during ordinary Buerger's exercises indicate that peripheral blood flow is definitely increased as compared with that in motionless limbs[9]. Exercises of the same type, done passively instead of actively, appear to have the additional advantage of avoiding the proximal vasodilatation which results from exercise and diverts a large amount of blood from distal ischemic areas. Furthermore, such passive exercises are the only ones possible for severely ischemic limbs that suffer intermittent claudication on active movements. Accordingly, a machine was devised that performs this service for such patients[10]. Preliminary results from the use of this type of device are encouraging.

Therapeutic implications

It seems obvious that ischemic limbs should never be raised above the heart level, but on the contrary should be lowered at times to a dependent position. By placing them alternately in a dependent and a horizontal position, the ill effects of continuous dependency can be avoided, while the beneficial effects on blood flow are retained. Passive raising and lowering of the limb appears to be preferable to active exercises in most patients with severe peripheral vascular disease. More work must be done to determine the long-range clinical effectiveness of this form of therapy.

8. (a) Uprus, V., Gaylor, J. B., and Carmichael, E. A.: Vasodilatation and Vasoconstriction in Response to Warming and Cooling the Body: A Criticism of Methods, Clin. Sc. 2:301-316 (Dec.) 1936.
(b) Roth, G. M., Williams, M. M. D., and Sheard, C.: Changes in Skin Temperatures of the Extremities Produced by Changes in Posture, Am. J. Physiol. 124: 161-167 (Oct.) 1938.
9. Wilkins, R. W.: Vasomotor Reserve, O. S. R. D. Contract OEMcmr 143, Progress Reports 9 and 10, 1943.
10. Wilkins, R. W.: Vasomotor Reserve, O. S. R. D. Contract OEMcmr 143, Progress Report 11, 1943.

Summary

Physiologic studies have been made of the circulatory effects of four different types of mechanical procedures applied to the limbs: venous occlusion, arterial compression, local compression, and alternate dependency and elevation.

Venous occlusion decreases blood flow distally while the venous pressure is increased. Arterial compression at certain selected pressures temporarily increases blood flow distally while the mean arterial pressure is increased, and before venous pressure rises high enough to impede blood flow. Compression of a limb reduces blood flow locally. Dependency of a limb increases blood flow; and alternate dependency and elevation to the horizontal level have a similar effect, but prevent the formation of edema. The implications of these results upon the treatment of peripheral vascular disease are discussed.

BIOPSY OF THE LIVER

NATHAN A. WOMACK, M.D.*

SAINT LOUIS

The importance of the liver in clinical medicine has been recognized since the days of antiquity. It was not, however, until recent years, when various functions of the liver began to be studied in detail, that the true significance of liver sufficiency began to be realized. Even now, this subject has not been completely explored. However, the development of physiologic facts and biochemical methods of studying function in the living patient have been of increasing value.

The morbid anatomist of a few decades ago, who classified diseases of the liver into various forms of cirrhosis, has now been superseded by the clinician, who studies the liver in its functional phase. The former made his observations on the far-advanced lesion associated with death. The latter studies the relatively early lesion in the living. Biologic and chemical experimentation is being correlated with structural change. For instance, the relationship of choline, methionine, and cystine to changes in the liver, both necrotizing and scarring, has been well investigated in animals. Dietary insufficiency involving certain of the vitamins has also been studied. Numerous poisons, both organic and inorganic, have been investigated. The effect of specific virus infestations in the liver has come up for considerable study, particularly during the past few years. The important part played by the liver in shock and in resistance to trauma and infections in general is now being investigated.

Tests of Liver Function

Most of the clinical studies have been made by the utilization of certain tests regarding the functional status of the liver. While many tests have been devised, they are all broadly related to a study of certain general functions of the liver. Among these functions are the excretion of bile pigment, the metabolism of various forms of sugar, the ability of the liver to conjugate substances that would otherwise be injurious, the excretion of phthalein dyes from the blood stream, the excretion of phosphatase, the formation of prothrombin, the esterification of cholesterol, the part played by the liver in the formation of plasma albumin, and the changes in the conjugation of plasma globulin. Often it is necessary to study the liver with various tests to determine the efficiency of some of the above functions. Such studies usually make it possible for one to state whether or not the liver is severely damaged. Often these tests will also give accurate information as to the nature of the damage.

Broadly speaking, these tests make it possible to differentiate between toxic destruction or inflammation in the liver parenchyma and pure mechanical obstruction of the bile ducts, either within the liver or in the extrahepatic system. Frequently, however, such obstruction of the hepatic duct is also associated with inflammatory changes within the liver and, as a result, the differential diagnostic value of such tests is greatly impaired. Again, many of these tests are too often not sufficiently discriminating, and their interpretation thus may be misleading.

Methods of Biopsy

Obviously, the diagnosis of liver dysfunction would be much easier if we were able to correlate findings in these functional tests with the morphologic and particularly cytologic changes that occur in the liver. It is not surprising, therefore, that considerable

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effort has been made to provide such correlation. The most accurate means of investigation would be a laparotomy in which the entire liver is exposed, examined grossly, and a small portion of it removed for microscopic study. Unfortunately, people who have severe liver damage become poor operative risks. The danger of anesthesia and surgical trauma is so great that in many instances such an exploration for diagnostic reasons alone is precluded. Furthermore, such a procedure is painful and the patient is subjected to a considerable hospital stay, which makes it economically inadvisable.

Study of the liver by use of the peritoneoscope has been recommended by many. This procedure too, however, has many shortcomings. Only the surface of the viscus can be observed, and the impression received from such inspection is often fallacious. Furthermore, no morphologic correlation is offered.

Since the development of needle aspiration of the liver a few years ago, much progress has been made. It is possible to aspirate, with relatively little danger, a small fragment of liver tissue, which can be studied microscopically. Another advantage of this procedure is that the physician can make repeated studies and follow the development of the lesion. It also has its shortcomings, however. Unless the liver is diffusely involved by the lesion, the biopsy may not be taken in the proper place. Where obstruction exists, the nature of the obstruction can not usually be determined. The study of lobular arrangement and relationships is likewise unsatisfactory.

Surgical removal of biopsy specimen

Several years ago, it occurred to us that in certain cases a biopsy specimen obtained surgically through a small incision made over the liver might afford more complete study of the liver than was possible with needle biopsy. Some of the results of this procedure are reported in this article.

A small incision, generally 4 to 6 cm. long, is made transversely over the margin of the right lobe of the liver. This is done with an anesthetic consisting of novocaine block combined with a basal anesthesia which is determined by the condition of the patient. The rectus muscle is split, the fibers gently separated, and the peritoneal cavity opened. With such an incision, it is possible to see a considerable portion of the right lobe of the liver. A finger can be inserted and even more of the liver palpated. It is possible to examine the gallbladder, to feel the common bile duct and pyloric region, the omentum, the right portion of the transverse colon, and the peritoneum. If ascitic fluid is present, it can be aspirated. It is fairly simple to remove one or more segments of liver tissue for microscopic study. Hemorrhage is never significant, and can be controlled with a single suture. The operative procedure takes only a few minutes and is not disabling. The postoperative discomfort is slight, and the patient generally never misses a meal.

So far, approximately 50 patients have been studied by this method. It has not been a routine procedure, but has been employed in cases where it was felt that a positive diagnosis was essential, and that a method should be employed which would not upset the patient too much.

The findings in several patients so examined are described briefly below. While the pathologic features in many of these cases are of great interest, complete classification of the pathologic findings will not be attempted at this time.

Presentation of Cases

Case 1

A 56-year-old white man was admitted to the Barnes Hospital in December, 1944. His chief complaint was nosebleed, which had been occurring off and on for approximately one year. He began drinking at about the age of 16, and had consumed from one quart to one gallon of whiskey per week for a number of years. For one year before admission he had had epigastric fullness and a yellow color in the whites of his eyes. He had been weak, and had lost 21 pounds.

On physical examination the patient appeared chronically ill and emaciated. His skin was slightly yellow. There was a generalized glandular enlargement of moderate degree. The chest was normal, except for a few moist rales at the bases. The liver could be palpated at the level of the umbilicus. It was firm, tender, and non-nodular. The remainder of the physical examination was within normal limits.

Laboratory data showed 2,800,000 red blood cells, 8 Gm. of hemoglobin, and 6,890 white blood cells in the peripheral blood. Differential examination of the blood smear revealed 27 normoblasts, 2 pronormoblasts, 3 reticulocytes, 2 myelocytes, 3 juveniles, 3 non-segmented polymorphonuclears, 28 segmented polymorphonuclears, 40 lymphocytes, and 13 monocytes. The picture suggested a leukemoid reaction, probably the result of carcinoma of the liver. The urine and stool were normal, the Kahn test was negative, the icterus index 20 units, cephalin flocculation test 3 plus. All other examinations were within normal limits.

The diagnostic problem presented here was to decide whether this patient had a carcinoma of the liver, cirrhosis of the liver associated with carcinoma, or cirrhosis of the liver alone. It was impos-

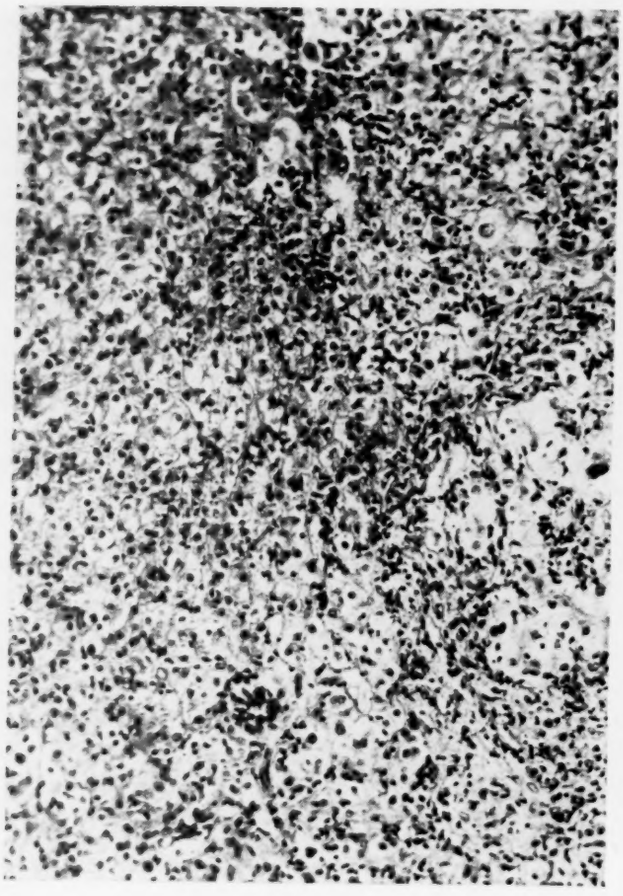

Fig. 1. Massive, fulminant liver damage.

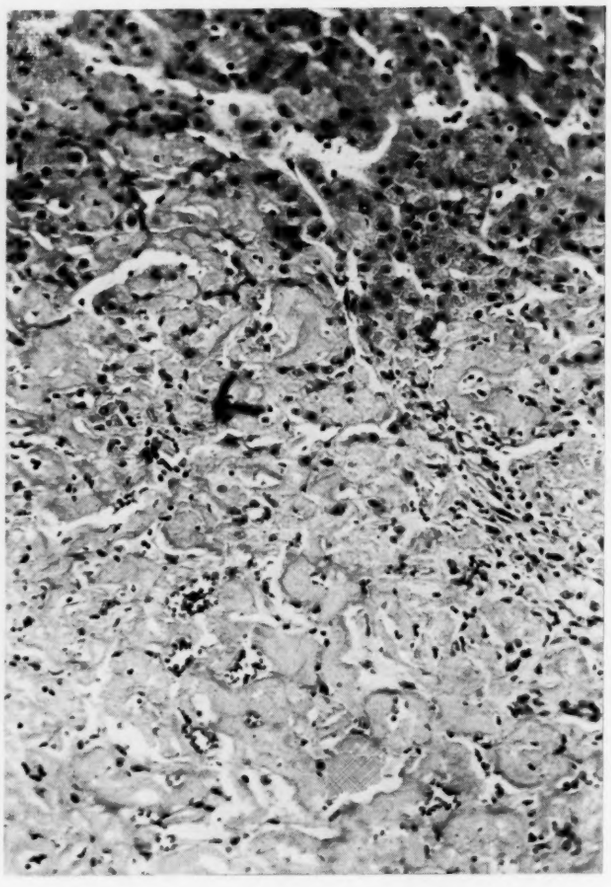

Fig. 2. This picture is one occasionally seen following the action of certain poisons upon the liver.

sible to make a differential diagnosis from the data at hand.

Accordingly, a segment of liver was removed for biopsy through an incision 5 cm. long made over the liver edge under local anesthesia. The liver was smooth, and no nodules were seen. Small, grayish lines could be seen very faintly throughout the liver.

The microscopic picture seen in the biopsy specimen (fig. 1) was one of diffuse hepatic degeneration, with scarring and inflammatory infiltration. There was a moderate amount of parenchymatous regeneration. The architecture of the hepatic lobules had become altered, and it was obvious that if this patient survived the acute degenerative phase of cirrhosis, a hobnail cirrhosis would eventually develop. The picture was highly suggestive of that produced by nutritional insufficiencies, with superimposed toxic damage.

The patient ran an intermittent fever for several weeks. He was given many transfusions, supportive vitamin therapy, and a high-protein, high-carbohydrate diet. On January 30, however, he began to bleed from the nose, lungs and intestinal tract, and died that evening.

Case 2

A 29-year-old single girl entered Barnes Hospital July 25, 1945, with a history of hypochromic anemia which had been present for about two years, in a mild form. This anemia had not responded particularly well to liver extract or iron. About six months before admission to the hospital, she began to note increased weakness. This gradually became more pronounced, until upon admission she was confined to her bed. There had also been considerable nausea, vomiting, and loss of appetite.

The important physical findings upon her admission to the hospital were limited to a slight enlargement of the liver, the edge being palpable 3 cm. below the costal margin, and evidence of recent moderate loss of weight.

The red blood cell count was 3,520,000 and the hemoglobin 10.6 Gm.; the white blood cell count was normal, as was the differential count. Repeated extensive studies of the bone marrow and peripheral blood failed to reveal any abnormality other than the mild anemia. The stool was guaiac-positive (1 plus). The urine consistently showed a 2 plus reaction for albumin. The blood protein, nonprotein nitrogen, and blood sugar were all normal. Repeated examination of the stool failed to reveal any parasites, although a moderate amount of blood was always present. The concentration diuresis test revealed a relatively poor ability to concentrate urine. The oral hippuric acid test was normal.

For diagnostic purposes it was thought wise to examine a segment of this patient's liver microscopically. Accordingly, on August 1, 1945, under local anesthesia, the liver was explored through an incision 5 cm. long over the edge. The liver was soft, brown, and mottled, but presented no nodules or increase in size. Microscopic examination of the biopsy specimen showed a rather characteristic picture (fig. 2) There were numerous focal areas resembling coagulation necrosis, such as is frequently noted in animals suffering from chronic carbon-tetrachloride poisoning.

When the patient was questioned further, she finally admitted that she had noted pinworms in her stool approximately a year ago, and that for

the past six months she had been taking medicine for this condition which she had procured from a local druggist. This medication was discontinued, and she responded rapidly.

Case 3

An 18-year-old white, unmarried female student entered the Barnes Hospital on May 17, 1945 and died on May 24. Her chief complaints were abdominal pain, distention, and malaise. Approximately four months prior to her admission she had noted the onset of generalized fatigue and malaise, which failed to improve even with adequate rest at night. About four weeks later she experienced a three-day episode of pain in the right flank which was made worse by deep inspiration. This subsided, but returned in three weeks. The malaise and weakness were associated with a loss of appetite but no nausea or vomiting. Approximately six weeks before admission the pain in the right flank returned, and tended to radiate to both shoulders. Two weeks prior to entry she began to detect gradual abdominal distention, and had frequent episodes of vomiting. She became faintly jaundiced, and for two days before admission had difficulty in voiding. There was no history of chills or fever. She had lost 7 pounds in weight.

The positive findings on physical examination were limited to the abdomen. The abdomen was tense, and shifting dullness was demonstrable in both flanks. The liver was palpated 10 cm. below the right costal margin; the edge was very firm, tender, and smooth. During the patient's stay in the hospital the liver gradually increased in size and the spleen became palpable.

Laboratory tests showed a moderate secondary anemia and an icterus index of 30. The cephalin flocculation test was negative and sternal marrow studies were normal. The stool was positive for stercobilin.

A differential diagnosis was difficult. The picture resembled a primary tumor of the liver, but this was thought unlikely because of her age and the acuteness of the lesion. The evidence of infection in the liver was slight, however, and the findings did not suggest a degenerative process. Accordingly, on May 23 a biopsy specimen was removed from the liver through a transverse incision made at the level of the umbilicus on the right side. A portion of the rectus muscle was severed, and the margin and undersurface of a very large liver were exposed. Approximately 1500 cc. of bloody fluid was aspirated from the peritoneal cavity. The liver was mottled, nodular, and hard. The nodules were dark yellow, and the picture grossly resembled either primary carcinoma or xanthomatosis. A small piece was removed for biopsy without bleeding. The wound was closed with interrupted silk sutures.

Microscopic studies of the tissue (fig. 3) showed a rapidly growing, diffiusely infiltrating primary carcinoma of the liver. There was very little evidence of scarring, and very little degeneration was present.

The patient died on May 24, and at autopsy there was found a primary carcinoma of the liver involving all lobes, with invasion of the small radicles of the portal and hepatic veins. Numerous small areas of metastatic carcinoma were seen in all the lobes of the lungs.

Case 4

A 58-year-old white male was admitted to the Barnes Hospital on September 16, 1944, because of a large inguinal hernia which he had had for some time. His past history indicated that he had had a penile lesion twenty years before, and was treated

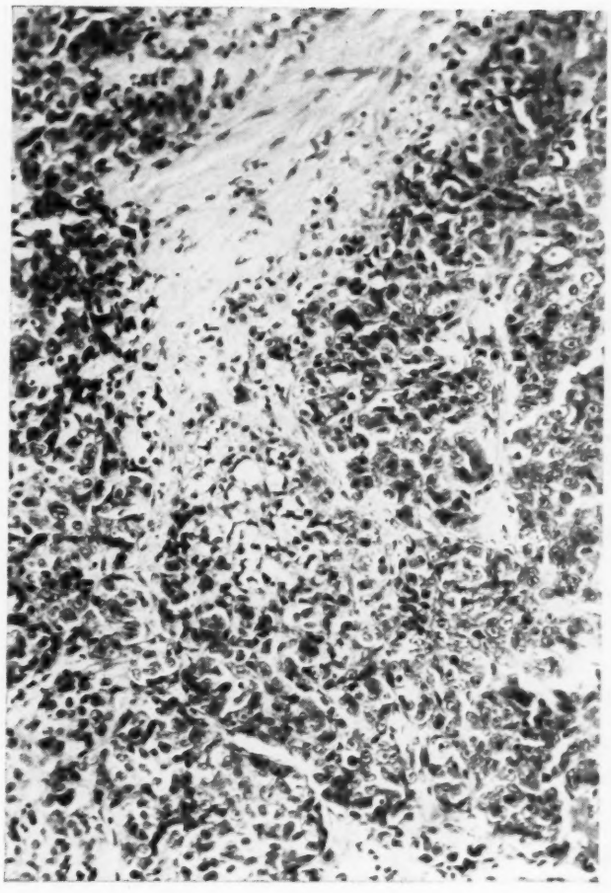

Fig. 3. A rapidly growing hepatic cell carcinoma.

with arsenic and mercury injections. He had had epilepsy for more than twenty years and he had been a heavy drinker for ten years, although more recently he had not had any alcoholic beverage at all. The hernia had been present for approximately ten years. About one year before admission he began to have anorexia and constipation, with a weight loss which amounted to 34 pounds. His extremities became very thin, and six months before entry his abdomen began to enlarge.

Upon admission to the hospital, his temperature, pulse and respiration were normal. The positive physical findings were limited chiefly to those relating to the abdomen. The patient, however, showed considerable emaciation; there were distended venules over the cheeks and nose, and he possessed "liver palms." While there was no cardiac enlargement, a systolic murmur was heard at the base of the heart and there were signs of fluid at the left lung base. The abdomen was distended and a definite fluid wave was noted on palpation. The abdominal veins were dilated, and the liver could be felt 4 cm. below the costal margin. There was a large scrotal hernia. No ankle edema was present.

Laboratory examinations revealed the red cell count, the white cell count and the hemoglobin to be normal. The nonprotein nitrogen was normal. The plasma proteins were 4.4 Gm. per 100 cc.—3.2 Gm. of albumin and 1.2 of globulin. The icterus index was 6 units, and an intravenous hippuric acid function test showed 59 per cent excretion. The Kahn test was questionably positive. Bronchoscopic examination showed evidence of external pressure on the left side. Cell studies of both pleural and peritoneal

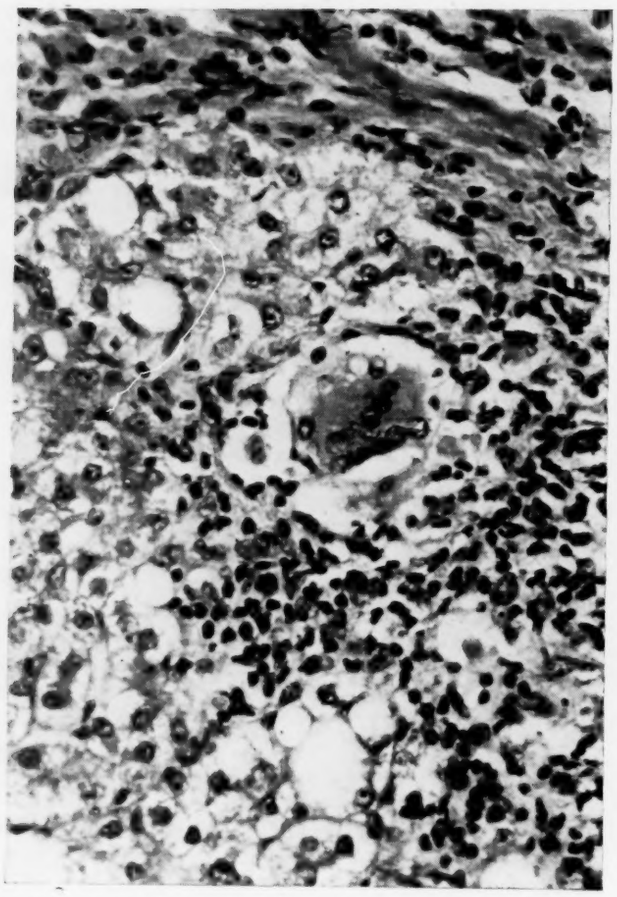

Fig. 4. The appearance here is typical enough of tuberculosis to warrant active efforts to demonstrate the organism.

fluid showed questionable adenocarcinoma; the findings were not characteristic enough for a positive diagnosis to be made.

Although the physical findings and history were highly suggestive of cirrhosis of the liver, the laboratory findings were not in keeping, and primary carcinoma of the liver could not be excluded.

On October 16, under local anesthesia, a 3-cm. incision was made over the liver edge. The peritoneum was entered and the liver came immediately into view. It was studded with small, pearl-gray nodules which were irregular, hard, and discrete, each nodule measuring about 3 mm. in diameter. Similar nodules were found on the omentum. One was removed from the omentum, and a block of liver containing one of these small nodules was excised. Figure 4 is a photomicrograph of one of these small nodules. One sees a fairly characteristic granuloma composed of lymphocytes, epithelioid histiocytes, and giant cells. In none of these granulomas was there caseation. The picture, however, was entirely suggestive of tuberculosis, and this diagnosis was subsequently confirmed by inoculation of pleural and ascitic fluids into guinea pigs.

Case 5

A 48-year-old colored male was admitted to the Barnes Hospital on October 12, 1944, sixteen months after he had first noted pain in the right upper quadrant. This pain first began in June, 1943, and was of a mild, recurrent type. In October, 1943, there had been an episode of jaundice while he was confined in a neighboring hospital with an illness diagnosed as bronchopneumonia. Since the onset of his pain he had become progressively weaker. In January, 1944, ten months before his admission to the hospital, he began to notice abdominal swelling and dyspnea. He saw his physician, who told him that his liver was enlarged. He lost 35 pounds of weight during the eight or ten months before admission. The abdominal distention and dyspnea had become progressively worse, and he had had nausea with vomiting on three occasions about three months before admission to the hospital. There was no pain associated with eating, and he had had no bloody or tarry stools or hematemesis. A history of improperly treated syphilis at the age of 22 was obtained.

On physical examination the pulse, respiration, and temperature were found to be normal. The patient was a poorly developed, emaciated, colored male with extreme abdominal distention, shifting dullness, and a fluid wave. Telangiectatic vessels were present over the left deltoid and right femoral regions. There was no jaundice. A soft systolic murmur was heard over the aortic area at the base; no thrills were present. There was a distended inferior epigastric vein along the costal margin. The abdomen was asymmetrical because of the presence of a bulging mass in the right flank. Palpation revealed a large nodule in the right flank which was apparently connected with the liver. The liver surface was nodular elsewhere and the edge, felt 15 cm. below the costal margin in the midclavicular line, was firm; the liver was very tender.

The red blood cell count was 3,500,000, the hemoglobin 10 Gm., the white cell count 12,500, with a slight shift to the left in the Schilling hemogram. The urine had a specific gravity of 1.008; a few granular casts and white cells were seen microscopically. The stool was guaiac-negative, and the blood Kahn was positive (40 units.)

During the patient's stay in the hospital two paracenteses were done and about 11,000 cc. of fluid was removed. This was a clear, yellow fluid with a specific gravity of 1.013. There were 340 cells present in a low power field before acetic acid was added, and it contained 2.1 Gm. of protein per 100 cc.; none of the cells appeared malignant. The cephalin cholesterol test was 1 plus; the total serum proteins were 6 Gm. per 100 cc.—3.4 Gm. of albumin and 2.6 of globulin. The bromsulfalein test showed 50 per cent retention after thirty minutes. Fluoroscopy gave a suggestion of enlargement of the ascending aorta at the base, but x-ray and barium swallow studies did not confirm this. Gastrointestinal x-ray examination was normal.

The differential diagnosis rested between syphilitic cirrhosis, carcinoma of the liver on the basis of cirrhosis, and hypertrophic nodular cirrhosis. The patient was given antisyphilitic treatment for two weeks with no improvement. A diagnosis being impossible to establish, Dr. Kemler removed a section of the liver for biopsy on November 4. This procedure was carried out through a small incision made in the upper right quadrant over the liver edge, under local anesthesia. The liver was noted to be nodular and lobulated, many of the lobules being as big as one's fist. There were huge veins running across the liver, and many dilated venules and arterioles. Several broad white scars were seen throughout the liver parenchyma. The liver was extremely large, extending in every direction as far as a finger could reach; it felt hard. Two biopsy specimens were taken.

Figure 5, which is a photomicrograph of one of the specimens, shows the picture of primary carcinoma of the liver parenchyma involving damaged liver cells. Studies of other portions of the specimens revealed a fairly classic type of Laennec's cirrhosis, upon which was superimposed carcinoma of the liver.

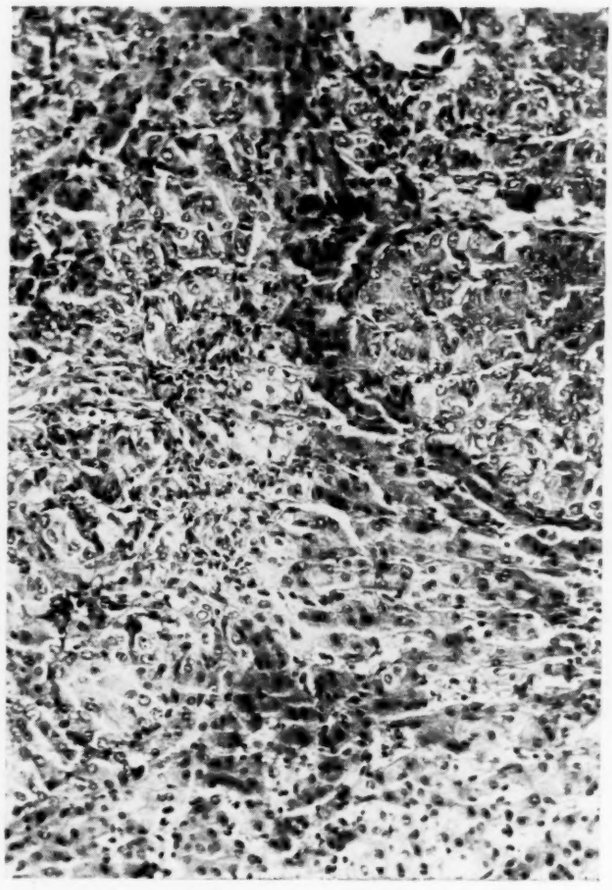

Fig. 5. Carcinoma of the hepatic cells arising in a liver previously damaged by cirrhosis.

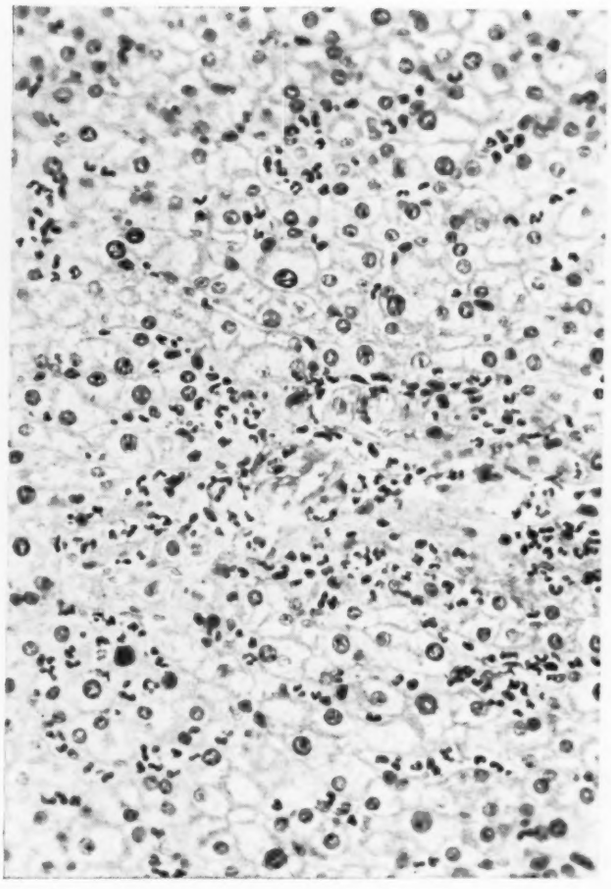

Fig. 6. This picture is that usually seen in diffuse pyogenic invasion of the liver secondary to some process draining into the portal system.

Case 6

A 28-year-old single girl was admitted to the Barnes Hospital for an operation to correct deformity of the nose. Without the surgeon's knowledge, she had been on a strict reducing diet of approximately 1200 calories for three months before entering the hospital. Although no liver function tests were performed before operation, the physical examination and routine laboratory findings were within normal limits.

The operation was a long one, requiring ether anesthesia for more than two hours. Forty-eight hours later she began to have pain in the right upper quadrant, radiating to her back. This rapidly became worse, and within a few hours was associated with chills and a temperature of 39.5 C. (103.3 F.). Marked rigidity and tenderness were present in the upper right quadrant. Her pulse rate became extremely rapid, and the blood pressure began to fall. She was given several blood transfusions.

A history of a severe enteritis a year before her admission to the hospital was obtained from her physician. The differential diagnosis lay between acute cholecystitis and an acute infectious process in the liver resulting from the previous enteritis, upon which was superimposed dietary insufficiency and a surgical procedure.

Because of her serious condition it was thought wise to make a small incision over the liver margin to investigate the condition of the gallbladder and the liver. The peritoneum was opened through a 5-cm. incision, and no free fluid was found in the abdomen. The liver was considerably enlarged, extending down almost to the umbilicus, and was extremely soft and mushy. The gallbladder, cystic duct, and common duct were normal, and there were no stones. The head of the pancreas was normal, as were the stomach and the first and second portions of the duodenum. The tissues around the kidney showed no evidence of infection. The only pathologic process that could be made out was in the very soft, large liver. Accordingly, a diagnosis of acute, diffuse pyogenic hepatitis was made, and a biopsy of the liver was made to verify this opinion.

Microscopic examination of the biopsy specimen showed the picture of acute inflammation (fig. 6). The sinusoids were filled with polymorphonuclear leukocytes, and the liver cells showed a picture resembling cloudy swelling. There was a granular change throughout the cytoplasm of the liver cells, together with considerable edema and poorly defined cell membranes. Many of the cells were vesicular and contained vacuoles. The nuclei varied considerably in size, and many of them showed evidence of acute degeneration.

Because of the diagnosis so made, it was possible to treat this patient effectively with antibiotics. Recovery was rapid.

Discussion

There is always considerable danger attached to the formulation of a rigid classification of diseases of an organ, when the nature of some of the diseases is poorly understood. With the present information that we possess, certainly this statement seems to be

true of the liver. There are many lesions that cannot be considered cirrhosis, that are not typical of acute yellow atrophy, that are not due to syphilis, and yet that are associated with necrobiosis, regeneration, and at times eventual scarring. Some of these lesions cause physiologic impairment of the liver, as determined by function tests, and others do not. In many instances there has been too little correlation between the function tests. This statement has been particularly true in cases of clinically early liver damage, before the appearance of jaundice, profound asthenia, or prostration.

In all of our cases where hepatic disease was eventually proved to be present, morphologic evidence of the disease has been found upon biopsy studies. Cytologic study of the liver therefore not only becomes important in rounding out our information about this organ, but may be an aid in the diagnosis of early lesions before certain of the function tests show alteration, and at a stage in which therapy may be effective.

The method of obtaining biopsy specimens that we are suggesting has the disadvantage that frequent repetition is undesirable, although we have found that multiple biopsies a week or two apart are feasible. It has the advantage, however, of giving a considerable amount of information—more than may be obtained so safely with any other method. If this information can be correlated with tests of physiologic function of the liver and the clinical and laboratory findings, much will be learned. An understanding of early changes in the liver becomes possible.

In this presentation we have selected a few characteristic cases from approximately 50 in which such studies have been made. They illustrate among other things the true diagnostic value of the procedure in differentiating primary cancer from cirrhosis of the liver, or cirrhosis complicated by cancer. Other instances could be cited in which metastatic carcinoma to the liver arising from silent foci in the gastrointestinal tract, and not apparent with the usual methods of examination, was recognized.

Conclusions

By the use of a small incision, approximately 5 cm. long, made over the liver edge under local anesthesia, it is possible to examine with a fair degree of thoroughness many of the viscera in the upper right quadrant. Visualization of a considerable portion of the right lobe of the liver is possible, as is the removal of one or more areas for microscopic examination. Out of approximately 50 cases in which this method of examination has been used, 6 are described in detail, and the microscopic findings are correlated with the clinical picture and physiologic tests of liver function.

This method of obtaining biopsy specimens has proved to be safe, simple, and effective in adding to our knowledge of the condition that exists in the liver, particularly in early derangements due to damage from nutritional and toxic disorders, inflammation, and tumors.

THE BRONCHIAL ARTERY IN PULMONARY INFARCTION

H. D. BRUNER, M.D.*

PHILADELPHIA

Perhaps because of its inaccessibility and deceptively small size, the importance of the bronchial artery has not been generally appreciated. Calling it the nutrient supply to the lung is an understatement, for the integrity of all the pulmonary structures depends on flow in this obscure vessel. Yet, with one exception, the pathologic physiology of diseases has never been definitely connected with defective bronchial artery flow[1]. The exception, formulated by Virchow on the basis of autopsy material and an experiment[2], links bronchial artery enlargement with embolism and restrictions of pulmonary flow. Since the affected parenchyma did not undergo ischemic necrosis, he inferred that bronchial artery flow was responsible for preventing breakdown of the infarct, and so began a still unsettled controversy.

The object of this paper, after a review of the meager literature on the bronchial artery in infarction, is to analyze the hemodynamics of the early stages of an infarct in the light of recent data on bronchial artery flow. Bronchial artery enlargement in congenital pulmonary artery anomalies is

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1. De Burgh Daly, I.: Interference of Intrinsic Pulmonary Mechanisms as a Potential Cause of Asthma, Tr. Med.-Chir. Soc. Edinburgh 115:139-144, 1935-36; In Edinburgh M. J. (Sept.) 1936.
2. Virchow, R.: Gesammelte Abhandlungen zur wissenschaftlichen Medizin, Exp. XX, pp. 285, 294, 295. Frankfurt a. M., 1856.

excluded[3]; vascular growth in the non-functioning lung *in utero* scarcely duplicates the vascular emergency of embolism. There is no need to dwell on the frequency of infarcts and the number which, giving few or no clinical signs, apparently heal without scarring[4].

Collateral Circulation in Pulmonary Infarction

A preliminary question to be considered is whether pulmonary artery collateral connections could support the area of infarction if the bronchial arteries were ligated. The available evidence indicates that they could *not*. First, many pulmonary infarcts proceed to necrosis despite the combination of bronchial artery flow and whatever pulmonary collateral circulation there may be[5]. Secondly, injection experiments on embolized lungs[6] show that the pressure of injection is the factor determining flow through the pulmonary collaterals, but that even high pressures do not give complete injection of the affected sector. With a suspension which will not pass capillaries, the sector remains uninjected. Clearly, the collaterals are of capillary size.

From the theoretical standpoint it may be predicted that pressure in the pulmonary arteries is too low to force blood through long sections of resistant capillary channels, particularly when pulmonary vein *ostia* of low resistance are so readily available. An early infarct does contain blood, but this could enter the infarcts as readily by retrograde flow from the veins as from the capillaries. It has been claimed that ligation of the bronchial artery made no difference in the pathologic changes following experimental embolism in dogs[7], but the validity of this experiment is doubtful; even if the ligature had chanced to include the main bronchial artery, the extrapulmonary collateral connections in the dog are so rich as to provide nearly normal blood flow[8].

Histologic Studies

Virchow's thesis stimulated search by histologic methods for possible anastomoses between bronchial and pulmonary systems, as new channels would hardly develop where connections already existed. Injections of either or both sets of vessels clearly showed that communications were present, but the details and areas were disputed for a number of years[3,6b,7,9]. Despite the innate deficiencies and highly abnormal hydraulics of the injection technique, such data were variously interpreted as proving or disproving that bronchial blood reaches the alveolar capillaries in quantities sufficient for the needs of the lung.

Miller's views of the vascular interrelations[9a] are shown schematically in figure 1. His careful reconstructions have been confirmed by radiographic and perfusion studies and injections into the living animal[6a,8,9b,10]. Bronchial artery flow enters the pulmonary system at two points: (1) the capillary bed on the respiratory bronchioles, and (2) the pulmonary veins, after perfusing its own capillary bed. In some species the visceral pleura is an additional fusion area. No true precapillary anastomoses between the two systems exist; what once were thought to be such are now recognized as *vasa vasorum* on the pulmonary artery derived from the bronchial artery[9]. Bronchial flow can reach alveolar capillaries only after it has passed a capillary bed.

To summarize, histologic methods of study have proved unsuitable for evaluating the hemodynamics of the two streams. Nevertheless, such accurate data are requisite for pathologic and physiologic studies.

3. Christeller, E.: Funktionelles und Anatomisches bei der angeborenen Verengerung und dem angebeborenen Verschluss der Lungenarterie, inbesondere ueber die arteriellen Kollateralbahnen bei diesen Zustaenden, Virchows Arch. f.path.Anat. 223:40-56, 1917.
4. Chasnoff, J.: Pulmonary Infarction, Bull. U. S. Army M. Dept. 6:125-139 (Aug.) 1946.
5. Castleman, B.: Healed Pulmonary Infarcts, Arch. Path. 30:130-142 (July) 1940.
6. (a) Mathes, M. E., Holman, E., and Reichert, F. L.: A Study of the Bronchial, Pulmonary and Lymphatic Circulations of the Lung under Various Pathologic Conditions Experimentally Produced, J. Thoracic Surg. 1:339-362 (April) 1932.
   (b) Karsner, H. T. and Ghoreyeb, A. A.: Studies in Infarction: III. The Circulation in Experimental Pulmonary Embolism, J. Exper. Med. 19:507-511, 1913.
7. Karsner, H. T. and Ash, J. E.: Studies in Infarction: II. Experimental Bland Infarction of the Lung, J. Med. Research 27:205-224, 1912.
8. Bruner, H. D. and Schmidt, C. F.: Blood Flow in the Bronchial Artery of the Anesthetized Dog, Am. J. Physiol. 148:648-666 (March) 1947.
9. (a) Miller, W. S.: The Lung, Springfield, Ill., C. C. Thomas, 1940.
   (b) Berry, J. L.: The Relation between Bronchial and Pulmonary Circulations in the Human Lung, Investigated by Radiopaque Injections, Quart. J. Exper. Physiol. 24:305-314 (Feb.) 1934.
10. (a) Horine, C. F. and Warner, C. G.: Distribution of the Pulmonary and Bronchial Circulation, J. Thoracic Surg. 2:80-86 (Oct.) 1932.
    (b) Berry, J. L. and de Burgh Daly, I.: The Relation Between the Pulmonary and Vascular Systems, Proc. Roy. Soc. s. B. London 109: 319-336 (Dec. 2) 1932.
    (c) De Burgh Daly, I. and von Euler, V.: The Functional Activity of the Vasomotor Nerves to the Lungs in the Dog, Proc. Roy. Soc. s. B. London 110:93-111 (Feb. 1) 1932.
    (d) Alcock, P., Berry, J. L., de Burgh Daly, I. and Narayana, B.: The Action on Perfused Lungs of Drugs Injected into the Bronchial Vascular System, Quart. J. Exper. Physiol. 26:13-27 (April) 1936.

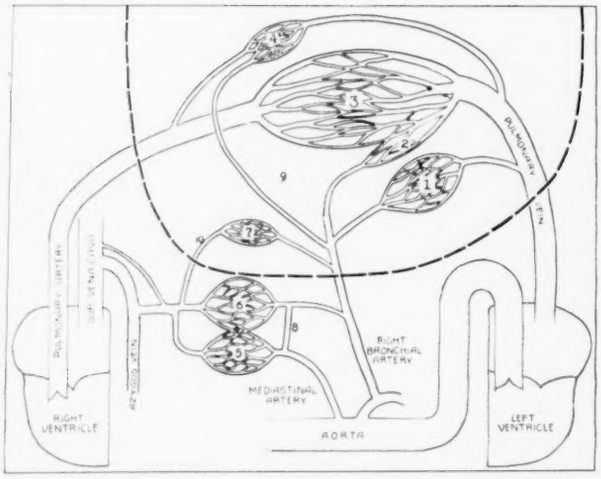

Fig. 1. Schematic diagram of the vascular connections of the right posterior bronchial artery in the dog. The heavy dashed line separates intra- and extrapulmonic portions. 1: Capillary bed of the general intrapulmonic flow. 2: Capillary bed on respiratory bronchioles showing fusion with 3: alveolar capillary bed supplied by the pulmonary artery. 4: Visceral pleural capillaries supplied by either or both systems; drainage in either case as shown. 5: Capillary bed of a mediastinal artery fusing with 6: capillary bed of extrapulmonic branches of the bronchial artery. 7: Capillary bed of intrapulmonic bronchial artery branches proximal to the first two or three dichotomies and in the perihilar pleura. 8: Collateral arterial channels. 9: Vasa vasorum on pulmonary arteries derived from the bronchial arteries; these were once claimed to be collateral connections. 10: True bronchial veins. —Reprinted from the American Journal of Physiology (8).

Pathologic Studies

Virchow's original observations have been confirmed in autopsy material[3], and, more important, experimentally[6a]. Injection of radiopaque material into the bronchial arteries of animals with experimentally infarcted lobes showed that: (1) Enlargement of the artery was true hypertrophy, not vasodilatation, and occurred within two to four days following embolism; (2) enlargement was restricted to the infarcted lobes, and hence was an effect of local conditions; (3) while inflammatory reactions to bacteria hastened and perhaps exaggerated the hypertrophy, it was basically independent of inflammation; (4) injected radiopaque material seemed to diffuse into the inflammatory region surrounding a *septic* embolus, whereas when the embolism remained *sterile* the enlarged bronchial artery filled cleanly throughout the infarct. The haziness surrounding septic emboli was interpreted as newly developed precapillary connections between the two systems, but it might also signify increased capillarity or capillary permeability.

From experiments following embolism or ligation of the pulmonary vessels, three observations are noteworthy[7,10a,11]: (1) Intense congestion and rapid deterioration of the lung followed restriction of pulmonary vein drainage, even though the pulmonary artery was also ligated; this finding parallels clinical knowledge that cardiac disease is likely to be complicated by necrotic pulmonary infarction. (2) The congestion following ligation of the pulmonary artery in normally breathing animals was absent during positive intratracheal ventilation. (3) Plugging of a main bronchus at the time of embolism resulted in inflammatory changes, followed by gangrene; these changes were absent when embolism of the pulmonary artery had occurred a month previously, and the bronchial artery had become hypertrophied.

To summarize, the pathologic studies have emphasized the importance of the bronchial artery and pulmonary vein in infarction, while minimizing that of the pulmonary artery. Infection and atelectasis are important factors in determining the outcome of the infarct. The pathologic literature shows a serious lack of data giving the percentage of infarcts which heal without residua, in contrast to those ending in necrosis. Neither have data been found showing that bronchial enlargement is always associated with healing of the infarct, while failure to enlarge is correlated with necrosis.

Physiologic Studies

Only two studies of the bronchial circulation by physiologic techniques have been reported. One employed simultaneous perfusion of the bronchial and pulmonary circulations of excised lungs[10b,c,d], and the other, direct flow measurements in the anesthetized dog[8]. Using the response to bronchoconstrictor and dilator drugs as an indicator of perfusion, the former experiments showed that, when the two systems were perfused at normal pressures, bronchial artery blood perfused the bronchioles to the exclusion of the pulmonary system. Changes of pressure and flow in the bronchial circulation generally caused pulmonary artery pressure to vary

11. (a) Kuettner: Beitrag zur Kenntnis der Kreislaufs Verhaeltnisse der Saugethierlung, Virchows Arch. f. path. Anat. 73:476-523, 1878.
(b) Underhill, S. W. F.: An Investigation into the Circulation through the Lungs, Brit. M. J. 2:779-782 (Nov. 12) 1921.

in the same direction, but sometimes the reverse or no effect was seen. Conversely, changes in the pulmonary artery pressure were without noticeable effect on bronchial pressure, although bronchial venous drainage shifted chiefly to the true bronchial veins when pulmonary artery pressure rose. Despite a lack of details, these experiments indicate that the pressures in the two systems are the foundation for the hemodynamic interrelations.

The direct flow measurements[8] were carried out in dogs, using the main right bronchial artery. The flow in this artery averaged 4.8 cc. per minute (range 1.0 to 26.7 cc per minute), which, corrected for extrapulmonary flow and computed for both lungs, came to 6.1 cc. per minute for the mean total bronchial flow draining into the pulmonary veins. Calculated in terms of simultaneous cardiac output (pulmonary artery flow), the total intrapulmonary bronchial artery flow averaged 0.3 cc. per 100 cc. of cardiac output; the maximal flow observed was 1.02 cc. per 100 cc. of cardiac output. Thus, on the average, some three hundred times as much blood circulates through a sector of lung by way of the pulmonary artery as by way of the bronchial artery; even when the bronchial artery flow was at its peak, the blood flow in the pulmonary artery was about one hundred times as much. At first glance this finding would seem to deny the possibility that bronchial flow might substitute even in part for pulmonary flow, but it is important that the bronchial flow was labile and influenced more by physiologic conditions than by anatomic measurements; furthermore, these measurements were not made in the hypertrophied artery.

Pathologic Physiology of Pulmonary Infarction

Let us now synthesize these data into a picture of what may happen after embolism of a large intralobar branch of the pulmonary artery. In view of the shortcomings of the data, theory bordering sometimes on speculation has been employed[12].

Distal to the embolus, arterial and capillary pressures become nearly equal to pulmonary vein pressure; the latter shows a respiratory fluctuation superimposed on the general pressure level, which is determined by left atrial pressure, and by resistance to the flow of blood entering proximal to the embolus. Blood tends to enter the infarct by three routes: (1) *The alveolar capillary network from collateral pulmonary artery radicles.* As previously stated, the high flow resistance and low pressure discounts this source; the pressure does not rise unless a lobe or more is infarcted[13]. (2) *The bronchial arteries.* A fraction of the flow proceeds past the embolus to the capillaries on the bronchioles which mesh with the alveolar capillaries; the latter, now that opposing pressure is minimal, are more deeply penetrated by bronchial flow. The other portion of bronchial blood passes directly into the pulmonary veins, and regardless of whether it increases venous pressure, it creates movement of venous blood toward the heart. If the bronchial arteries carry more blood than usual, as is suggested by the steeper pressure gradient and possibly by local vasodilatation, vascular hypertrophy would be expected. (3) *The pulmonary veins.* The alveolar capillaries, responding to the alternating respiratory pressures[14], may extrude and receive blood from the pulmonary veins which function as a reservoir; this pool of blood is not stagnant (see below). Of these three sources, the bronchial artery provides the only positive flow into the infarct. The "white infarct" found at autopsy falsely suggests an absence of blood.

Assuming that blood does enter the infarct, the next question is whether the volume of flow is large enough to maintain the lung tissues not normally supplied by the bronchial artery. Ordinarily one's estimate would be based on the adequacy of exchange of oxygen and carbon dioxide, but in the lung, so long as air moves in and out, alveolar gaseous metabolism is independent of blood supply. Therefore, the lung's *non-gaseous* metabolic requirements are determinative. These, to judge by the low rate of oxidation found in excised lung tissue[15], might easily be met by a restricted flow or by any other means of keeping the local metabolite concentration within reasonably physiologic limits. A joint effect of the pulmonary vein reservoir, the bronchial flow, and the res-

12. In so doing we recall Dr. Manning's favorite advice: "Light a candle; don't ignore the darkness."

13. Gibbon, J. H., Jr., Gibbon, M. H. and Kraul, C. W.: Experimental Pulmonary Edema Following Lobectomy and Blood Transfusion, J. Thoracic Surg. 12:60-77 (Oct.) 1942.

14. Macklin, C. C.: Evidences of Increased Capacity of the Pulmonary Arteries and Veins of Dogs, Cats and Rabbits, during Inflation of Freshly Excised Lung, Rev. canad. biol. 5:199-232, 1946.

15. Stadie, W. C.: Personal communications, 1944, 1947.

piratory variations may make it possible for the small flow of fresh blood to perfuse the infarct out of proportion to its actual mass. In a manner analogous to the way in which a fresh-water stream forms an estuarial zone of intermediate salinity with the ocean, the ebb and flow of blood from the capillaries may extend to the veins. When this "dead space" blood is mixed with fresh bronchial blood, an intermediate metabolite concentration is obtained, and simultaneously some of it is discharged toward the heart.

Thus the bronchial artery dominates the mechanisms apparently responsible for meeting the metabolic needs of the infarct. The presumed small volume of flow in the artery need not deny its importance in infarction, so long as unusual demands—for example, gaseous exchange—are not made of it. The fact that not all pulmonary infarcts end in necrosis indicates that the total blood supply into the area *can* be adequate. Subsequent increase of the bronchial fraction, as evidenced by hypertrophy of the bronchial artery, probably improves blood supply to the optimal rather than the adequate level.

The obverse question is equally important: Why do certain pulmonary infarcts proceed to necrosis? Several self-evident factors are listed; their effects appear self-propagating. (1) Anatomic deficiency of the vascular setup may limit the above sources of blood. (2) Obstruction of the bronchi causes the oxygen requirements to be thrown on the blood flow; experimental data demonstrate that embolism sets up bronchoconstrictor and secretory reflexes which obstruct the airway[16]. (3) Pulmonary congestion from mitral lesions or decompensation may retard blood flow both into and out of the infarct; acute deterioration of the lung, however, is likely to follow any pre-existing depressed status. (4) Bacterial contamination of embolic or hematogenous origin, by giving rise to toxins or "spreading" factors, would disrupt the continuity of the vascular bed; local edema compressing neighboring vessels, direct endothelial damage, and induction of blood coagulation lead to the same effect. The central physiologic lesion in all these conditions is tissue anoxia, followed by nuclear degeneration, cellular dissolution, leukocyctic invasion, and repair by scar tissue[5].

16. Jesser, J. H. and de Takats, G.: The Bronchial Factor in Pulmonary Embolism, Surgery 12:541-552 (Oct) 1942.

Obviously definite answers to the questions raised are not warranted. As an opinion, however, it is probable that the bronchial circulation is the chief reason why many pulmonary infarcts do not undergo ischemic necrosis.

Summary

Recent data on bronchial artery flow are considered in relation to Virchow's claim that it is responsible for the survival of infarcted pulmonary tissue. An analysis of the probable hemodynamic and metabolic status of the uncomplicated pulmonary infarct indicates that the flow, while small, is not inconsistent with this theory.

CONGENITAL CYSTS OF THE LUNG

Report of Two Cases

JULIAN A. MOORE, M. D.*

ASHEVILLE

Congenital or acquired cysts of the lung are not common, and for that reason are often mistaken for other conditions. Congenital pulmonary cysts may cause symptoms shortly after birth, in childhood, or in adult life. They may be discovered unexpectedly, on roentgen examination or at autopsy. When pulmonary cysts are confused with other pulmonary lesions, improper management results in prolonged disability and invalidism.

The purpose of this paper is to report 2 cases of infected pulmonary cysts which illustrate the diagnostic difficulties and the therapeutic problems presented by such cysts after they become infected.

Case 1

An 11-year-old girl from Alabama was admitted to Biltmore Hospital on June 17, 1938, with a chief complaint of cough and expectoration of foul sputum.

Her present illness began December 26, 1934 (when she was 7 years of age), with a respiratory infection which was diagnosed as influenza and pleurisy. A few days later her physician detected physical signs of a pleural effusion in the left side of her chest. He referred her to a surgeon, who aspirated this side of her chest, and obtained a thin, pinkish fluid.

A thoracotomy by rib resection was done; tube drainage was maintained for ten weeks, and was then discontinued in April, 1935. The wound healed,

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and she remained well except for a hacking cough, which was thought to be due to diseased tonsils. A tonsillectomy was done in 1936, but the cough continued. In March and April, 1938, she ran a low-grade fever, and her mother noticed that her breath had a foul odor. On April 10, 1938, she suddenly spat up a large quantity of foul pus, and had continued to do so. About this time, her mother first noticed clubbing of the fingers. She had had no illness except measles prior to the onset of her present illness.

Physical examination revealed a well developed girl of 11, who did not appear very ill. The fingers and toes showed moderate clubbing. There was diminished expansion of the lower half of the left side of the chest. The percussion note was flat below the eighth rib anteriorly and the fifth thoracic vertebra posteriorly. Over this area the breath sounds were absent, and the voice sounds were not transmitted. The scar of the former thoracotomy was present. The hemoglobin was 68 per cent, the erythrocyte count 3,650,000, and the leukocyte count 11,200. The posterior-anterior and lateral roentgenograms (fig. 1 and 2) showed a rounded cavity in the base of the left side of the chest, containing air and fluid. Examination of her sputum revealed fusospirochetes and many mixed organisms, but no tubercle bacilli. A diagnosis of a chronic empyema with a broncho-pleural fistula was made by me.

On June 30, 1938, a thoracotomy was done by resecting a portion of the tenth rib in the scapular line. When the parietal pleura was incised, no free pleural space was encountered, and no empyema was found, although pus had been obtained by aspiration at this site. Pus was again aspirated, and the thin wall of what appeared to be a pulmonary abscess was incised. A considerable amount of putrid pus was aspirated. In my operative notes, I stated that the wall of the abscess was smooth, glistening, and red. No necrotic tissue and no trabeculations were seen. This appearance is not typical of a pulmonary abscess, and made me believe that this was an infected cyst of the lung, which would subsequently require lobectomy. A portion of the wall of the cyst was removed for examination. The pathologist did not recognize the true nature of the lesion.

The patient had a very stormy convalescence. A high fever developed, and she was extremely ill. A roentgenogram revealed a density in the left upper part of the chest, which was proved to be a mesial empyema. This was drained by a closed thoracotomy in the fifth interspace posteriorly on July 26. The pus removed was putrid and contained fusospirochetes and mixed organisms. After this procedure the girl gradually improved, and was discharged from the hospital on August 18, 1938. Continuous drainage of the infected cyst was maintained by means of a rubber tube.

The patient remained well, attended school the next year, and returned to Biltmore Hospital on June 2, 1939. Roentgenograms showed the same rounded cavity at the left base without a fluid level.

On June 3, 1939, the left phrenic nerve was crushed under local anesthesia. On June 5, under intratracheal cyclopropane and ether anesthesia, a lobectomy of the left lower lobe was attempted. The lobe was found to be densely adherent; it was freed with difficulty and with considerable loss of blood. By the time the lobe was separated from the diaphragm and the chest wall, the patient began to show signs of shock. Bleeding vessels were ligated; a gauze pack was inserted, and the wound partly closed. She rallied quickly after a transfusion of whole blood.

On June 19, under intratrachael cyclopropane and ether anesthesia, the lobectomy was completed.

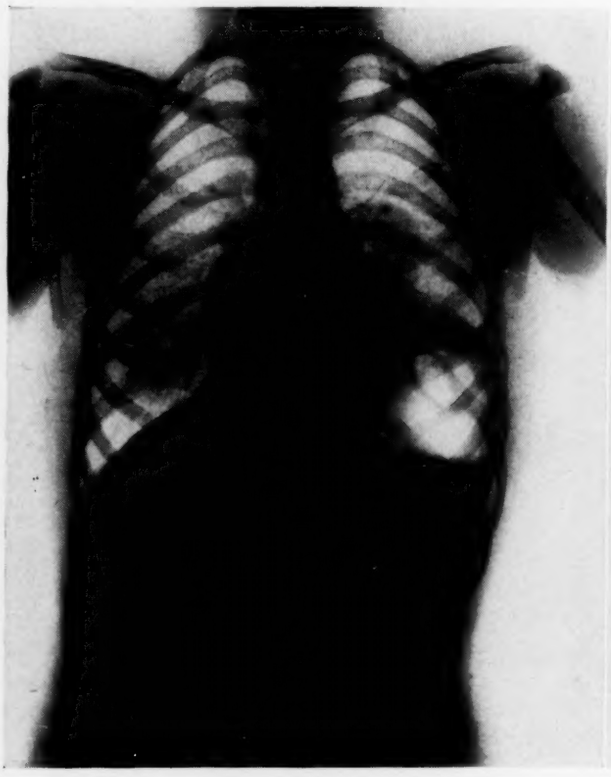

Fig. 1. (Case 1) Posterior-anterior roentgenogram, showing a large cavity in the left lower thorax, with a fluid level.

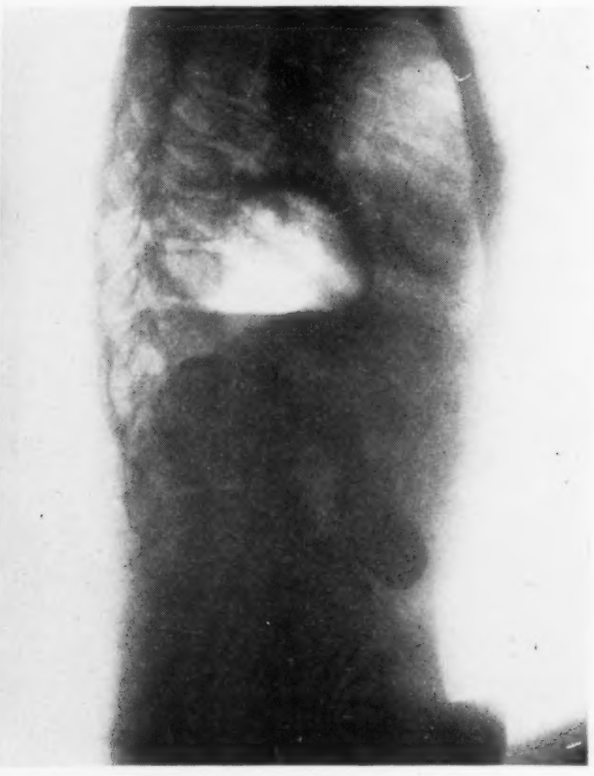

Fig. 2. (Case 1) Lateral roentgenogram, showing the same cavity occupying the space of the left lower lobe. Notice the absence of inflammatory zone around the cavity.

Again difficulty was encountered in dissecting the lobe free from the mediastinum and upper lobe. The dissection was accomplished without the loss of too much blood, and the lobe was removed by the tourniquet technique. Since blood continued to ooze, the pleural cavity was packed with gauze, and the wound partly closed. The patient showed signs of mild shock, but this was controlled with a blood transfusion.

The pathologist's report was as follows: "The mass of lung tissue measures 3 by 6 inches, and contained a smooth wall cavity occupying almost the entire area, leaving a shell of collapsed lung tissue from 0.5 to 1 cm. in diameter. Microscopically the lining of the cyst wall is made up of a layer of granulation tissue, in which numerous polymorphonuclear leukocytes, lymphocytes, and plasma cells are seen. There is no epithelial lining to be seen. Throughout the wall of the cyst one sees collapsed bronchioles with peribronchial fibrosis and lymphocytic infiltration. Collapsed alveoli are seen in which there are many desquamated endothelial cells and pigmented monocytes. There is no evidence of tuberculosis or malignancy."

Her recovery was rapid. The gauze pack was gradually removed, and on June 23 a rubber drainage tube was inserted. On July 3 she was discharged from the hospital; and on September 3, 1939, the drainage tube was removed, as the pleural cavity was obliterated. This patient is now a grown young lady attending college.

Comment

This patient, I believe, had a true congenital cyst of the left lower lobe, which became infected at the age of 7, and which was erroneously diagnosed and treated as empyema. It subsequently became reinfected, and was mistaken for a chronic empyema, with a broncho-pleural fistula. Yet the roentgenograms (fig. 1 and 2) are characteristic of a cyst. Note that the cavity is round. There is no inflammatory zone around the cavity, as you would see in pulmonary abscess or in tuberculosis. Note that the pleura is not thickened, as would be the case in chronic empyema. At the time of my first operation, the true nature of the condition was recognized, and the cyst was drained. After the patient had recovered from the infection, lobectomy was successfully performed.

Case 2

A 20-year-old woman was admitted to Biltmore Hospital on July 24, 1946.

At the age of 10 this girl had pneumonia and pleurisy on the right side. Since then she had frequently had pleuritic pain in the right upper part of her chest. During the winters she had repeated episodes, consisting of pain in the right side of the chest, fever, and a non-productive cough. During the winter before admission she had a respiratory infection, diagnosed as influenza. It was accompanied with right-sided pleuritic pains and a non-productive cough. Since this episode, she had been listless and had fatigued easily. About July 1, 1946, pain developed in the right shoulder and right side of the chest. She was treated with diathermy, but did not improve.

A roentgenogram (fig. 3) was made, and interpreted as showing an atypical pneumonia. She was admitted to the hospital and treated with sulfadiazine and penicillin. A week later there was no change in the roentgenogram. At the onset, there was a small amount of rusty sputum. On the evening of July 25, 1946, while I was examining her, she began to cough severely and expectorated several ounces of thick, purulent sputum, which did not have a foul odor. After that, she continued to cough, and raised 60 cc. of sputum daily.

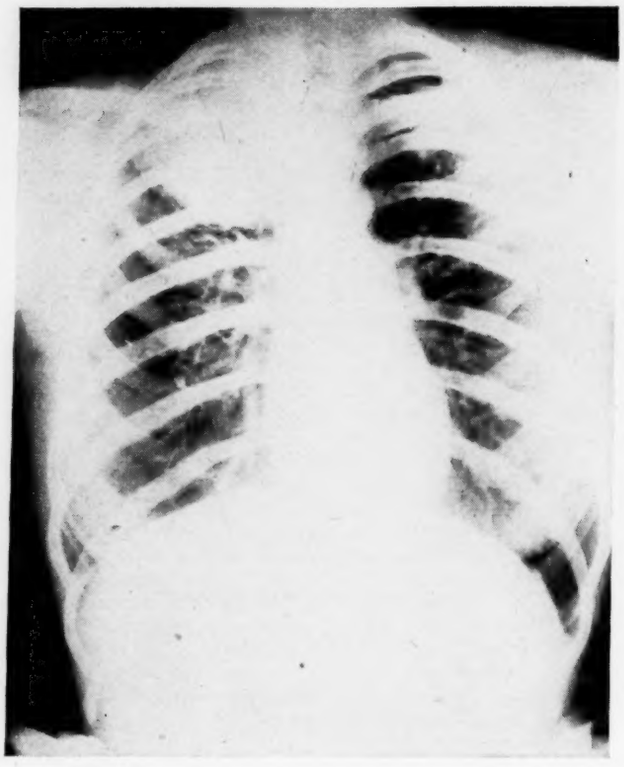

Fig. 3. (Case 2) Posterior-anterior roentgenogram, showing a heavy density in the right apex with a clear-cut border.

On admission, her temperature was 99 F., pulse 80, respiration 16. Physical examination revealed a well developed young woman, who did not appear to be very ill. The examination was entirely normal except over the upper lobe of the right lung, where there was dullness to percussion, absent breath sounds, and transmitted voice sounds.

Her hemoglobin was 88 per cent, the erythrocyte count 5,000,000, the leukocyte count 17,400. The differential count showed 59 per cent neutrophils, 4 per cent eosinophils, 35 per cent lymphocytes, and 2 per cent mononuclears.

Examination of the sputum revealed pneumococci and staphylococci. Repeated examinations were negative for tubercle bacilli. A tuberculin test, 1:1000, gave a 1 plus reaction.

The patient began to have fever ranging from 99 to 103 F. Under penicillin therapy it subsided in eight days. A bronchoscopic examination on August 5 yielded no information except that pus escaped from the right upper lobe bronchus.

Roentgenograms made on July 26 (fig. 4 and 5) revealed the true nature of the lesion. The density in the right upper part of the chest had disappeared, revealing a thin-walled cavity without a surrounding inflammatory zone. A diagnosis of an infected congenital cyst was made. As soon as the infection had been controlled, primary lobectomy was elected as the treatment of choice.

On August 8, 1946, under intratracheal cyclopropane and ether anesthesia, the right upper lobe was

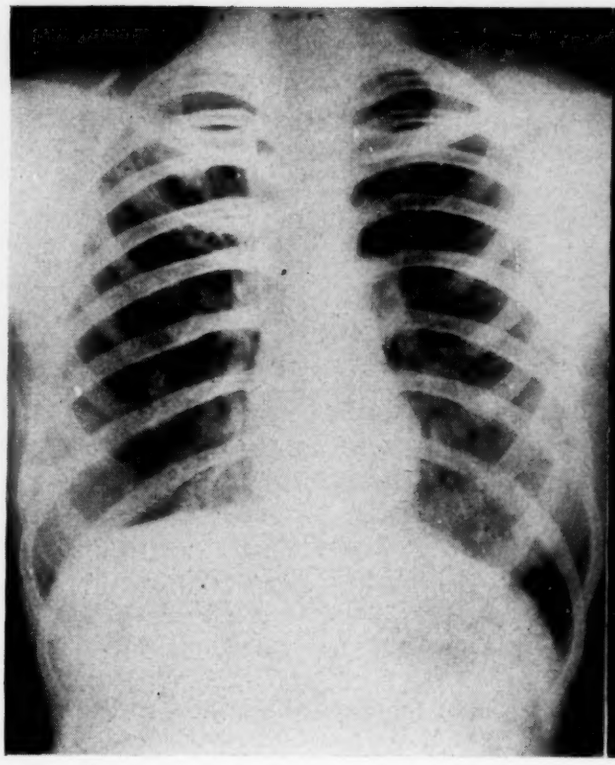

Fig. 4. (Case 2) Posterior-anterior roentgenogram, showing a large cavity containing a small amount of fluid at the right apex.

Fig. 5. (Case 2) A lateral roentgenogram which shows a large oval cavity in the right upper lobe containing air and a small amount of fluid

In figures 4 and 5 note the absence of thickened pleura and of a zone of inflammatory reaction around the cavity.

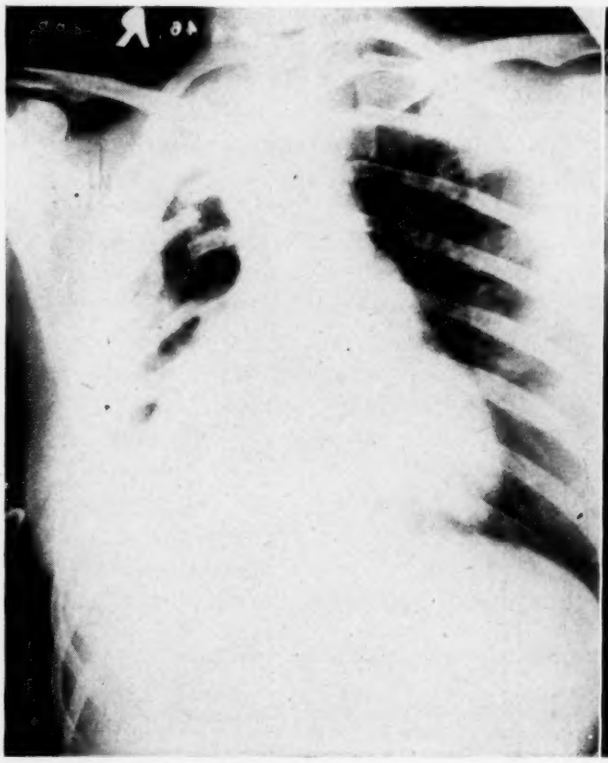

Fig. 6. (Case 2) Posterior-anterior roentgenogram which shows the right lower and middle lobes collapsed, the chest wall contracted, and the parietal and visceral pleura to be very much thickened.

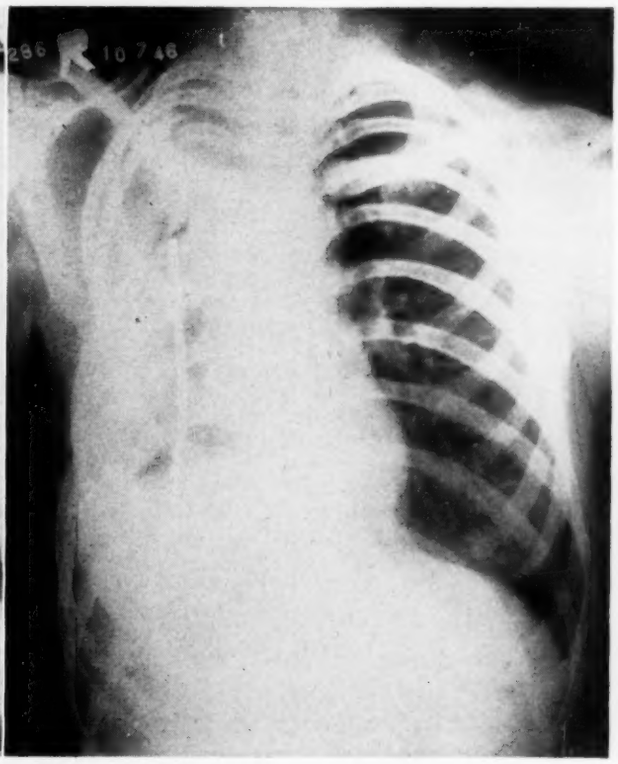

Fig. 7. (Case 2) Posterior-anterior roentgenogram which shows the lower and middle lobes re-expanded and a small empyema space in the apex, with the drainage tube in situ.

removed by the individual ligation technique. Five hundred cubic centimeters of blood was given by transfusion during the operation. She stood the operative procedure well.

The pathologist's report was as follows:

"The specimen consists of lung tissue which measures 12 by 8 by 5 cm. and contains a cavity 5 cm. in diameter. This cavity has formed a globular mass, the wall of which on one side is thin and on the other side is thick, and consists of lung tissue containing very little air. The lining of the cavity is grayish brown and relatively smooth.

"Microscopically, the wall of the cavity shows a lining of respiratory epithelium, which is interrupted in a few places. The wall is composed of dense, fibrous tissue, with rather extensive infiltration of chronic inflammatory cells, especially under the epithelium. Immediate adjacent lung tissue is more or less fibrosed and infiltrated with chronic inflammatory cells. There are areas that are typical of old, organized pneumonia. Immediately adjacent to the cavity are several compressed bronchioles. Many bronchioles contain an exudate of inflammatory cells. There are occasional areas of necrosis, but nothing suggesting tuberculosis.

"Diagnosis: Infected cyst of the lung."

Her convalescence was smooth until August 21, when her temperature reached 103 F. Some serosanguineous fluid was aspirated on several occasions, and was negative on culture. After each aspiration, 50,000 units of penicillin was instilled into the chest cavity. She continued to run fever, however; and in spite of the negative cultures and a low leukocyte count, I felt that she had empyema.

On August 29, a thoracotomy by rib resection was done. Two rubber tubes were inserted, a small one for irrigation and a larger one for drainage. The patient's temperature immediately came to normal, and she did very well except that she complained of considerable pain in the right side of the chest. The lower lobe showed no evidence of re-expansion. Repeated roentgenograms (fig. 6) showed that the pleura was becoming thicker, and that the right chest was contracted. This girl now had chronic empyema, and was well on the way to becoming a pulmonary cripple.

On September 19, under intratracheal cyclopropane and ether anesthesia, the original incision was reopened, and a complete decortication of the parietal and visceral pleura was done. Immediately the lower and middle lobes expanded, as the anesthetist applied positive pressure. A Pezzar catheter was inserted in the sinus of the thoracotomy wound and a no. 14 catheter into the first interspace in the midclavicular line. The operative wound was closed tightly. Within five days the lower catheter was blocked by the re-expanded lower lobe, and was removed.

Recovery from this operation was not as rapid as expected. The patient had several episodes of fever, but gradually improved, and was discharged from the hospital on October 31, 1946. Fig. 7 shows that the lower lobe has re-expanded to fill nearly the whole chest, there being a small pocket at the apex which has not closed.

Comment

This patient had a typical cyst, filled with fluid, which evacuated itself. Before the cyst evacuated itself, the x-ray appearance suggested a tumor. Afterwards it showed the characteristic picture of a cyst containing air. The cyst was rounded, the wall was thin, and there was no inflammatory zone around it.

In this patient, the proper treatment was carried out. Unfortunately empyema developed as a postoperative complication, and only an early decortication of the lung saved the patient from being a pulmonary cripple.

Maternal Welfare Section*

ABORTIONS AND THEIR MANAGEMENT

Abortion is defined as the termination of pregnancy prior to the twenty-eighth week or the time of viability of the fetus. Abortions are usually further subdivided into those which occur before the sixteenth week of pregnancy and those from the sixteenth to the twenty-eighth week. The greatest problem presented to the Committee on Maternal Welfare has been in the complications resulting from *early* abortions. After a pregnancy has reached four and a half months, the labor of the patient is considered with the same respect by the patient and the physician as a term pregnancy, and adequate care is usually arranged for the delivery.

The laity have little appreciation of the danger associated with spontaneous or instrumental termination of pregnancy in the early months. The records of the Maternal Welfare Committee contain twenty-four deaths which have resulted from complications of early abortions. Four of these resulted from the ingestion or injection of toxic drugs in an attempt to produce abortion. Nine were due to hemorrhage and eleven to infection following the termination of pregnancy. Three of the patients lost their lives after an attempt was made to interrupt pregnancy on a therapeutic basis.

A review of these records shows that practically all of the deaths were preventable and that ignorance or neglect on the part of the patient or her family was often responsible for the death. This factor was common in cases where criminal abortion was performed and the patient concealed her illness until it was too late for anything to be done. However, gross errors in judgment and tech-

*Prepared for the Maternal Welfare Committee of the Medical Society of the State of North Carolina:

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nique of the management of the patient are found in the records, which show the need for standard practices in the handling of the various problems presented.

Etiology

The etiology of traumatic or instrumental abortions is obvious, and the only problem is whether the procedure was carried out under criminal circumstances in an undesirable environment or whether asepsis was observed in a hospital.

The etiology of spontaneous abortion is a moot question, and numerous theories have been advanced. The most clearly established etiologic factor is that so carefully studied by Streeter[1] and Hertig[2], who have shown fetal abnormalities due to defective germ plasm or improper implantation of the ovum in approximately 40 per cent of all aborted products of conception. Imperfect implantation results in deficient nutrition and development of the embryo, with fetal death. The other various textbook theories of the etiology are held in considerable doubt by many observers. That endocrine deficiency may cause spontaneous abortion is probable, but the presence of such deficiency should be established for each patient concerned, if that is possible. Congenital uterine anomalies and uterine hypoplasia are probably much less significant than is suggested by the texts. Maternal disease, including renal lesions and syphilis, often cause abortions to occur.

Classification

Abortions are classified in a number of different ways. The etiology and the presence or absence of infection have a great influence on the prognosis and method of management. The following classification is complete:

Time	Etiology	Clinical Condition	
Early	Spontaneous	Threatened	
		Inevitable	Septic*
Late	Induced	Incomplete	
	a. Therapeutic	Complete	Non-septic
	b. Criminal	Missed	

*All abortions are potentially infected.

A careful history and physical examination are essential to an accurate classification of the lesion present. Accurate diagnosis must be made if serious errors in the management of the case are to be avoided. The patient's history should be carefully taken and an accurate estimate of the duration of pregnancy obtained. The presence or absence of fever and an estimate of the total amount of blood lost by the patient should be carefully considered in the decision as to how the problem should be managed. We must keep in mind that ectopic gestation and tubal rupture or abortion are common lesions which often result in the patient's death if an error in diagnosis is made. A careful, sterile pelvic examination is indicated in each case, and a presumptive diagnosis without examination is acceptable only if a careful examination has been made a few days before the onset of typical symptoms of a threatened abortion.

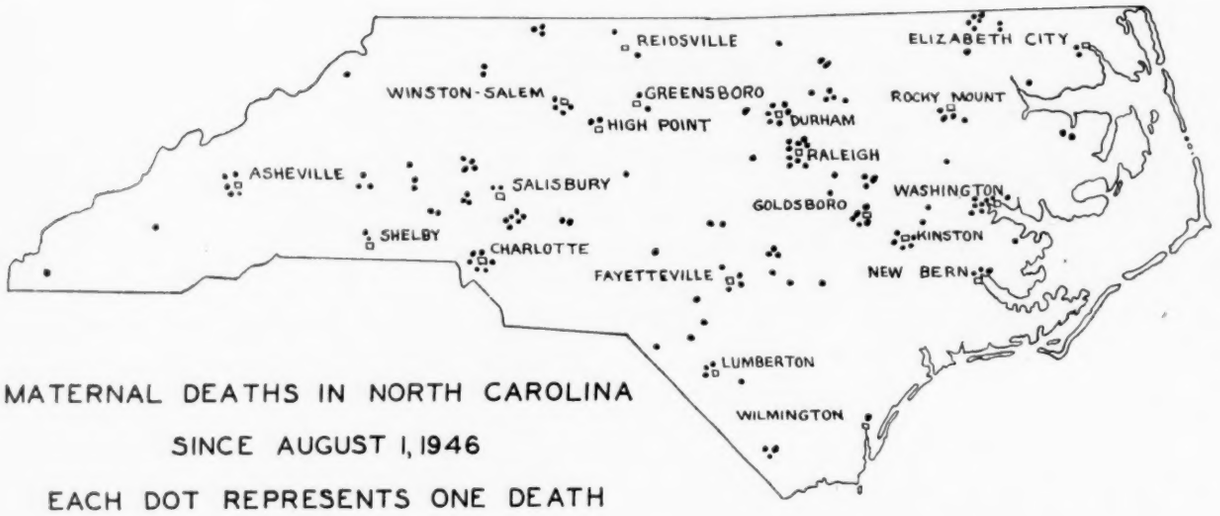
Diagnosis

The diagnosis of *threatened abortion* is justified when slight bleeding and lower abdominal cramps occur in the early weeks of pregnancy. A pelvic examination which confirms the presence of intrauterine pregnancy and the origin of the bleeding from the uterine cavity, with the escape of blood from the cervical canal, is essential to confirm the diagnosis. The adnexa must be carefully palpated to rule out the presence of tubal ectopic gestation. A diagnosis of *habitual abortion* is justified only if three spontaneous abortions are known to have occurred.

The presence of free bleeding, dilatation of the cervix to 2 cm. or more, or rupture of the amniotic sac which is confirmed justifies the diagnosis of *inevitable abortion*. An *incomplete abortion* is present if a clear history of passing parts of the products of conception—usually the fetus—is obtained, if bleeding continues, and if the uterus is enlarged by the retained placental tissue. Bleeding stops when an abortion is complete, and the uterus returns to near normal size.

A *missed abortion* is present when there is conclusive evidence that the fetus has been dead for sixty days. This diagnosis is justified when careful palpation and exact measurement show no growth of the uterus, and when the Friedman test is negative.

1. Streeter, George L.: Focal Deficiencies in Fetal Tissues and Their Relation to Intrauterine Amputation, Carnegie Inst. of Washington, 22:1-44, 1930.
2. Hertig, A. T. and Livingstone, R. G.: Spontaneous, Threatened and Habitual Abortion: Their Pathogenesis and Treatment, New England J. Med. 230:797-806 (June 29) 1944.



Treatment

Threatened abortion

The various forms of treatment recommended by numerous investigators of the problem of threatened abortion have obtained approximately the same results. It is apparent from the available publications that selection of the patient has had more influence upon the ultimate results than the method of treatment. The lay public is now educated to seek therapy for threatened abortion, and most such patients demand an active program of treatment when the wish for a child is present. The combined use of estrogen and progestin is at present the most popular method of endocrine therapy, but should not be instituted or continued over a period of time without pelvic examinations to confirm the presence of pregnancy and continued normal development of the uterus. Persistent or severe pain is strongly suggestive of ectopic gestation, and the presence of anemia or its appearance in the course of the patient's illness should always raise the question of this possibility.

Habitual abortion

Habitual abortion is primarily a problem of the specialist, and should be treated before conception takes place.

Inevitable abortion

This problem can usually be solved by the administration of oxytocic drugs. Pitocin and ergotrate preparations can be safely used in the first twelve weeks of pregnancy, and the administration of 0.5 cc. of posterior pituitary extract, repeated in thirty minutes and followed by the oral administration of six ergotrate tablets (one every four hours), usually results in the prompt spontaneous evacuation of the uterus. At times free bleeding requires the instrumental removal of the products of conception. Under these circumstances strict asepsis should be observed, and the cavity of the uterus evacuated as gently as possible, using sponge holders or similar very dull instruments. Usually the products are lying in the cervical canal and may be gently removed without invading the uterine cavity.

Incomplete abortion

Incomplete abortion should be handled in an identical manner. The presence of fever, evidence of instrumentation, or of pelvic contamination or infection is an absolute contraindication to invasion of the uterine cavity with any instrument, unless bleeding is profuse enough to endanger the patient's life. Under these circumstances the remaining contents of the uterus should be removed with as little manipulation as possible and by the gentlest possible use of the instruments.

The routine use of dilatation and curettage of the uterus is unnecessary for the majority of patients with incomplete abortion, and simply increases the danger to the group who have contamination of the pelvic tissues or latent pelvic infection. A careful general examination should precede the administration of any anesthetic agent. Marked anemia should be treated by the transfusion of an amount of whole blood sufficient to return the patient's hemoglobin to normal or near normal levels. All anesthetics are contraindicated in the presence of severe ane-

mia, and a fatal result may follow the administration of an anesthetic agent.

Complete abortion

No treatment is indicated for a complete abortion, except possibly the administration of an oxytocic drug to hasten involution of the uterus and as a prophylactic measure against bleeding.

Missed abortion

Conservatism is indicated in the presence of a missed abortion. If the patient is reassured about her condition and told that spontaneous termination of pregnancy will occur in time, the best results will be obtained. Attempts to evacuate the uterus are associated with appreciable danger, unless every safeguard, including blood for transfusion, is available.

Infection resulting from abortion

Adequate chemotherapy is indicated at the first definite evidence of pelvic infection associated with an abortion. A culture of the offending organism made from the cervical canal is of unlimited value in determining the prognosis and the most suitable drug for the patient's treatment. Transfusions are urgently needed by the anemic patient, as chemotherapy may be of little avail in the presence of even moderate anemia. If sulfonamides are to be used for the treatment of a pelvic infection, the dose should be regulated by determinations of the blood level of the drug; frequent blood counts should be done; and an alkaline urine should be maintained by the administration of 8 to 12 Gm. of sodium bicarbonate daily, or larger doses if they are necessary to produce an alkaline urine. An initial dose of 4 Gm. and maintenance doses of 1 Gm. every four hours are usually necessary to produce effective blood levels of a sulfonamide. Twenty thousand units every four hours is the minimum dose of penicillin which can be expected to produce good results. Larger doses of penicillin, up to 100,000 units every four hours, are necessary at times to control a pelvic infection. The drug which is used and the dosage must be largely determined by the offending organism and the severity of the patient's infection.

Summary

In summary it may be stated that abortion is one of the principal causes of maternal deaths in North Carolina. A program of lay education is needed to combat the problem. Standard practices, which are outlined above, should be employed in the management of this complication of pregnancy. Early and adequate transfusions of whole blood must be given if unnecessary deaths are to be avoided.

Therapeutic abortion is a dangerous procedure which should be carefully considered and employed only after thorough general preparation of the patient. Three recent deaths offer mute condemnation of the injudicious use of this valuable medical method. The subject of therapeutic abortion will be considered separately in an early issue.

Army Medical Officers Find Real "Shell Shock" Cases

Real "shell shock"—a relatively rare condition—has been found by Army medical officers. It is a hitherto undescribed medical syndrome—a mental and physical condition due entirely to the effect of blast on the tissues of the brain.

In World War I, practically every neuropsychiatric case resulting from combat was labelled "shell shock" until it was discovered that many such cases had never been within miles of an exploding shell. This made the term meaningless and it was dropped altogether from medical language, although it persisted among the lay public.

Now the existence of a limited number of cases of pure shell shock—now called "closed head injury syndrome due to blast"—is established by an intensive study reported in the October issue of the **Bulletin**, official Medical Corps publication.

The main complaints of the blast group were headache, ringing in the ears, deafness and anxiety. Other symptoms included dizziness (not true vertigo), daze and confusion, sudden attacks in which everything went black, weakness, fatigue, chest pains and backache. Apathy, mental lethargy and many physical complaints were also reported.

When seen two to twelve months after injury the syndrome complex was little changed. Ringing in the ears had disappeared in some cases and deafness had improved considerably. Backaches, dizziness and blackouts still were mentioned frequently. When questioned, none of the men would acknowledge retention of even 75 per cent normal energy. A third indicated poor memory for recent events but in none was memory loss a disability. Moderate depression was noted in several.

"In the total synthesis a more concrete concept of the syndrome emerges," the report said. "The men had been stunned and often rendered unconscious by nearby blast. Two thirds of the group had been unconscious. A third showed ruptured ear drums. Anxiety tension or dullness and apathy were present in 65 per cent. Headaches were heterogeneous in character. They were usually described as a 'dull ache' or sharp jabs of pain in the scalp. About 20 per cent showed minor but definite neurological changes."

Whether there is definite alteration in the brain has been impossible to determine, the report stated. The indications are, however, that this is true. Even so, the study explains, it need not cause any permanent mental or nervous disability and on the whole the prognosis for shell shock is good.

THUMBNAIL SKETCHES OF EMINENT PHYSICIANS

JOSIAH C. TRENT, M.D., F.A.C.S., *Editor*

DURHAM

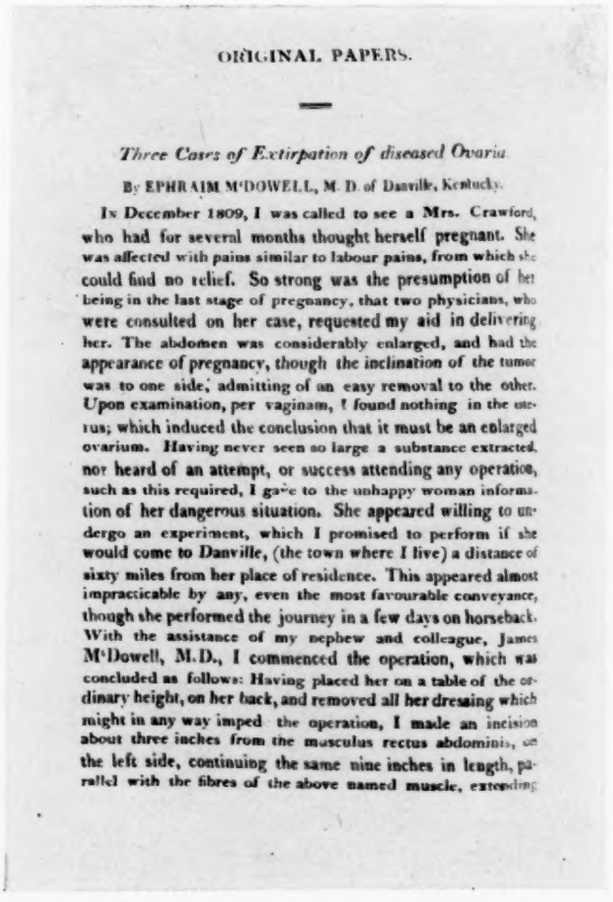
OBSTETRICS AND GYNECOLOGY IN AMERICA

V

EPHRAIM McDOWELL AND OVARIOTOMY

The story of the first ovariotomy, performed in December, 1809, in Danville, Kentucky, is a familiar one to most Americans. We have read many times of the courage and endurance of Mrs. Crawford, the patient, and of the skill and daring of the surgeon, Ephraim McDowell. For twenty-five tense minutes, McDowell proceeded with an operation which he knew to be a hazardous experiment; he knew also that failure would probably result in the destruction of his professional reputation. With no precedents to guide him, with no aid from anesthesia or asepis, with none of the elaborate paraphernalia of the modern operating room, he depended solely upon his own cool judgment and his accurate knowledge of anatomy. Twenty-five days later, Mrs. Crawford returned to her home, able once more to resume her accustomed routine.

Of the many stories told about McDowell's history-making operation, those that describe an indignant mob gathered at the house at the time of the operation, those that say he performed the operation elsewhere than in his own surgery, those that represent him as seeking to be spectacular are decidedly apocryphal. At the time of this famous operation, Ephraim McDowell, Virginia-born, Kentucky-bred, and Edinburgh-trained, had been in practice about fourteen years and was a respected member of his small community. His closest friends described him as a silent, phlegmatic man. His accomplishments grew, not from a desire for recognition or acclaim, but from the ingenuity, resourcefulness, and courageous attitude developed in him by long practice under the stern conditions of the frontier. He had derived inestimable inspiration, also, from the teachings of John Bell at Edinburgh, and it is interesting to note that both Bell and McDowell were made unhappy during the latter part of their lives by the small-mindedness and jealousy of their contemporaries and colleagues.



ORIGINAL PAPERS.

Three Cases of Extirpation of diseased Ovaria.

By EPHRAIM M'DOWELL, M. D. of Danville, Kentucky.

In December 1809, I was called to see a Mrs. Crawford, who had for several months thought herself pregnant. She was affected with pains similar to labour pains, from which she could find no relief. So strong was the presumption of her being in the last stage of pregnancy, that two physicians, who were consulted on her case, requested my aid in delivering her. The abdomen was considerably enlarged, and had the appearance of pregnancy, though the inclination of the tumor was to one side, admitting of an easy removal to the other. Upon examination, per vaginam, I found nothing in the uterus; which induced the conclusion that it must be an enlarged ovarium. Having never seen so large a substance extracted, nor heard of an attempt, or success attending any operation, such as this required, I gave to the unhappy woman information of her dangerous situation. She appeared willing to undergo an experiment, which I promised to perform if she would come to Danville, (the town where I live) a distance of sixty miles from her place of residence. This appeared almost impracticable by any, even the most favourable conveyance, though she performed the journey in a few days on horseback. With the assistance of my nephew and colleague, James M'Dowell, M.D., I commenced the operation, which was concluded as follows: Having placed her on a table of the ordinary height, on her back, and removed all her dressing which might in any way impede the operation, I made an incision about three inches from the musculus rectus abdominis, on the left side, continuing the same nine inches in length, parallel with the fibres of the above named muscle, extending

Fig. 1. The opening page of McDowell's article on his first three successful ovariotomies, as it appeared in the **Eclectic Repertory**, Philadelphia, 1817. (Reproduced through the courtesy of the Army Medical Library)

Mrs. Crawford's case was reported in 1817 in the *Eclectic Repertory* of Philadelphia (fig. 1), along with two other successful ovariotomies. The article immediately excited Dr. James Johnson of London to acid ridicule of McDowell's literary style; the Londoner also expressed total disbelief in McDowell's statement that he had found the patient engaged in making her bed on the fifth postoperative day. (The early mobilization practiced in this case by McDowell was considered new fifty years ago, when many of the greater German surgeons had their patients walk back from the operating room, and it is a recognized practice today.) We can better appreciate Dr. Johnson's incredulous reaction to the McDowell article when we realize that in those times both patient and surgeon regarded even a simple operation with terror and desperation, and

that for a surgeon to enter the abdominal cavity deliberately was unheard of. The same Dr. Johnson was giving expression to the general attitude of the medical profession when he wrote in a later review of ovariotomy: "In despite of all that has been written respecting this cruel operation, we entirely disbelieve that it has ever been performed with success, nor do we think it ever will." It seems almost unbelievable that a man could bring himself to oppose the strongest convictions of his colleagues as boldly as McDowell did in resolving to attempt ovariotomy.

It would seem that great achievements in medicine, such as McDowell's ovariotomy, frequently follow a definite pattern: A desire for achievement, the courage and energy necessary to perform a daring experiment, and inspiration, usually acquired from an outstanding preceptor. McDowell's teaching had been adequate; he possessed courage and ingenuity; and he proceeded with great deliberation to perform his task. He was prevailed upon to report his first three cases, however, only by much persuasion and after a lapse of seven years. Such caution and deliberation are virtues in medicine, all too often neglected today.

McDowell's pioneering effort earned for him the title, "father of abdominal surgery." He was followed in America by other courageous men, such as Nathan Smith, Goldsmith, and Rogers. The introduction of anesthesia in 1846 initiated a second epoch in the history of ovariotomy; the operation was no longer a novelty, but a common proceeding. Nevertheless, there continued to be long debates *pro* and *con*, and not inconsiderable feuds. The Atlee brothers (1843-1883) of Philadelphia became the great proponents of ovariotomy. One of them, Washington L. Atlee, in spite of his skill and renown, was forced to deliver an address revealing the indignities to which he had been subjected by other surgeons. One of his colleagues, on passing his house on Arch Street, said, "There lives the greatest quack in Philadelphia." Another remarked, "'Tell Dr. Atlee that I will not meet him in consultation because he undertakes to perform operations not recognized by the profession." One eminent surgeon, in 1851, went so far as to open his lecture with the following irrelevant words: "Gentlemen, it is my painful duty to announce to you that a respectable lady who, a few days ago, came from New York to this city with an ovarian tumor which was removed by Dr. Atlee, returned to that city today a corpse."

In spite of such opposition the practice of performing ovariotomy continued to spread in the United States and abroad. Cazeaux, in France, for six months had a battle on his hands in regard to the treatment of ovarian tumors; opposing him were such great names as Velpeau, Cloquet, and Trousseau. Most of the German school favored the operation, but even a few distinguished German surgeons continued to speak of it as sheer murder. Dr. Emiliani of Bologna, Italy, may perhaps be credited with being the first European ovariotomist[1] and second in the world to McDowell; in 1815 he removed an ovarian tumor 9 by 5 cm. from a 26-year-old woman, a baker's wife of "lymphatic temperament." The patient survived not only the operation but also the blood-letting, tartar emetic, hemlock, and other remedies, and thereafter produced six children in undaunted succession!

When Dr. J. Marion Sims was president of the American Medical Association, the sum of ten thousand dollars was requested for a "McDowell Memorial Fund" to be used in awarding prizes for the best essays written on diseases and surgery of the ovaries. A remark made then to the effect that Americans are very prone to lose sight of the teachings and examples of their men of genius seems to have been borne out, for by 1876, only one hundred and fifty-four dollars had been collected toward this fund! Only during the past thirty years has due tribute been paid to McDowell in any form of extensive writings and recognition; at the opening of the Duke Hospital in 1930 his name was given to the women's surgical ward. Kentuckians, at least, valued the memory of this great benefactor, and erected a small obelisk to honor him in the little town of Danville, Kentucky.

ROBERT N. CREADICK, M.D.
Duke Hospital,
Durham.

1. A German named Chrysmar may possibly have priority over Emiliani.

The rate of patient turnover in all VA hospitals has risen to a monthly average of more than 45 per cent because of improved medical care.

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MAY, 1947

DR. ISAAC H. MANNING

But for unavoidable obstacles the Manning issue would have been published in February, the month which marked the first anniversary of Dr. Manning's death. It is quite fitting, however, that it should follow so closely the annual meeting of the Medical Society of the State of North Carolina. During his lifetime Dr. Manning was such a large part of North Carolina medicine that he is sorely missed at all convocations of North Carolina doctors.

Dr. Manning served as president of the State Medical Society in 1933, and as its secretary during the unexpired term of Dr. Tom Long, in 1942. While he achieved more than ordinary success in many fields—as a teacher, as a physician, and as an administrator—he is probably remembered by most doctors for having conceived the idea of the Hospital Saving Association—the first hospital insurance plan sponsored by a state medical society—and for having nurtured it through its infancy to sturdy maturity. Had he lived, no doubt he would have felt that North Carolina's medical care plan represents further growth of his brain child.

Those who wrote the tributes to Dr. Manning which form the prologue to this issue were acting as spokesmen for "his boys" who began their medical careers under his tutelage. They spoke not only for his former students, however, but for the many other friends who loved him: he was too big to be claimed exclusively by those whose fortune it was to have him for a teacher.

* * * * *

THE VIRGINIA BEACH MEETING

This month, for the second time in its history, the Medical Society of the State of North Carolina held its annual meeting outside the state. While the decision to meet at Virginia Beach was made from necessity rather than from choice, most of those who made the long pilgrimage to attend felt well repaid. The drawback of distance was reflected in the attendance. Only 444 were registered — just half the number who came to Pinehurst last year, and, except for the Bermuda cruise meeting, the smallest attendance for the past twenty years.

The House of Delegates transacted a tremendous amount of business in its two lengthy sessions on Monday. President William Coppridge, in a clear-cut report to the House, listed the noteworthy legislative achievements of the past year as follows: (1) the adoption by the legislature of the medical care program; (2) the agreement of the nurses to modify, temporarily at least, their demand for an all-nurse board of examiners; (3) the passage of a bill to license practical nurses who have had one year's hospital training; (4) the defeat of "the perennial osteopath bill"; and (5) the defeat of the naturopath bill.

President Coppridge stressed the need for improvement in the present organization of our Society. To this end he recommended the employment of a full-time executive secretary, but stated that since this man would be a layman, he should work under the super-

vision of the secretary-treasurer of the Society, who is now and who should always be a physician. Another recommendation was that a committee of at least fifteen members, with each medical school represented, should be appointed and should hold quarterly meetings. The function of this committee should be to consider ways and means for making our Society's organization more efficient. Dr. Coppridge also stressed the importance of enlisting the younger men in the work of the Society, since they will eventually have to take over the responsibility for organized medicine in the state.

Dr. Roscoe McMillan's report as secretary-treasurer was encouraging. The membership of the Society has reached an all-time high of 2,073, and forty county societies have every physician in the county enrolled as a member. It was gratifying to learn that the NORTH CAROLINA MEDICAL JOURNAL made quite a respectable profit for the Society last year.

Among the highlights of the House of Delegates meeting was the report of Dr. Ivan Procter, secretary of the Board of Examiners. The board has met five times within the past year, and has granted licenses to 232 applicants.

A prolonged discussion took place over the relation of the Society to the Industrial Commission. As a result of the recommendations offered by the two committees reporting on this subject, headed by Drs. J. P. Rousseau and G. W. Murphy respectively, it is probable that some rather radical steps may be taken to improve, if possible, the status of doctors who do a considerable amount of industrial work. The responsibility for further action is left largely with the executive committee.

Dr. Hubert B. Haywood, chairman of the legislative committee, reported that more than one thousand bills had been introduced in the 1947 legislature, but that no legislation unfavorable to the medical profession was passed. He asked that he be relieved of the chairmanship of this committee, since he felt that he had carried the burden long enough. His report, carrying with it his resignation, was accepted, with thanks for the faithful service he has rendered.

A resolution was offered from Robeson County to amend the By-Laws so that the county officers of each society might take office in April or May, instead of January. The reason given for this proposed change was that the new officers should have the benefit of attending a state meeting by way of preparation for their task. This resolution was unanimously adopted.

Since the transactions of the House of Delegates will be published in the August issue, no attempt has been made to give an exhaustive summary of the proceedings.

The First and Second General Sessions were well attended, and the close attention paid was a tribute to the excellence of the papers presented. Most of the papers read at these sessions and in the section meetings will be published in later issues of the JOURNAL.

The climax of the meeting was the President's Night banquet and dance. As an innovation this year the President's Address was given at the banquet instead of at the First General Session. This change met with universal approval, and President Coppridge's address was enthusiastically received. It will be published in the June issue of the NORTH CAROLINA MEDICAL JOURNAL.

The nominating committee took their responsibility seriously, and their report seemed satisfactory to all. Dr. James F. Robertson of Wilmington was chosen as president-elect. Other officers elected were: Dr. V. K. Hart of Charlotte, first vice president; Dr. J. G. Raby of Tarboro, second vice president; Dr. G. G. Dixon of Ayden and Dr. J. LaBruce Ward of Asheville, members of the State Board of Health for the next four years; and Dr. L. R. Hedgpeth of Lumberton, member of the Hospital Saving Association.

Dr. P. W. Joyner of Enfield, Dr. Alban Papineau of Plymouth, and Dr. Harry Johnson of Elkin were designated delegates to the Medical Society of Virginia, and Dr. Frank Ward of Lumberton, Dr. C. H. Pugh of Gastonia, and Dr. Lewis Gaskin of Albemarle were named delegates to the South Carolina Society. Delegates to Georgia are Dr. Robert Mathews of Greensboro, Dr. W. A. Hoover of Murphy, and Dr. Ben Kendall of Shelby. The Tennessee delegation consists of Drs. B. O. Edwards, Westbrook Murphy, and S. L. Whitehead, all of Asheville.

INDIANA SETS A GOOD EXAMPLE

The midwestern states have long been noted for their independent thinking in various matters, especially in politics. This spirit of independence is exemplified in a resolution recently adopted by the Indiana Legislature, and inserted in the *Congressional Record* for February 10. The resolution might well be adopted by our own state, among others. It is short enough and important enough to be quoted in full:

"Indiana needs no guardian and intends to have none. We Hoosiers—like the people of our sister States—were fooled for quite a spell with the magician's trick that a dollar taxed out of our pockets and sent to Washington, will be bigger when it comes back to us. We have taken a good look at said dollar. We find that it lost weight on its journey to Washington and back. The political brokerage of the bureaucrats has been deducted. We have decided that there is no such things as 'Federal' aid. We know that there is no wealth to tax that is not already within the boundaries of the 48 States.

"So we propose henceforward to tax ourselves and take care of ourselves. We are fed up with subsidies, doles, and paternalism. We are no one's stepchild. We have grown up. We serve notice that we will resist Washington, D. C., adopting us.

"**Be it resolved by the House of Representatives of the General Assembly of the State of Indiana (the Senate concurring),** That we respectfully petition and urge Indiana's Congressmen and Senators to vote to fetch our county courthouse and city halls back from Pennsylvania Avenue. We want government to come home.

"**Resolved further,** That we call upon the legislatures of our sister States and on good citizens everywhere who believe in the basic principles of Lincoln and Jefferson to join with us, and we with them, to restore the American Republic and our 48 States to the foundations built by our fathers."

EDITORIAL NOTES ON THE NINETY-THIRD ANNUAL SESSION

The Officers' Breakfast at 7:30 Tuesday morning was well attended. The fact that every seat at the table was occupied is a tribute to our secretary-treasurer. The officers of the county societies could not help but gain inspiration from the addresses of Dr. Hugh McAllister of Lumberton, who presided, President Coppridge, President-Elect Frank Sharpe, and Dr. Joseph S. Hiatt, president of the Hoke County Medical Society.

Comments were heard on all sides about the excellent service given by the Cavalier Hotel and by the other hotels on the beach. This was in contrast to the hurried and harried atmosphere of the Carolina Hotel last year. One member of the Auxiliary expressed this feeling quite well when she said, "Last year at Pinehurst we were treated like boarders; here we are treated as guests."

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Perhaps the greatest ovation given during the meeting was received by Mrs. Paul McCain, after Secretary Roscoe McMillan had presented her to those present at the banquet Tuesday night. This was a spontaneous demonstration of the affection and admiration which the doctors and their wives have felt for her and her late husband.

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The two members of the editorial board of the NORTH CAROLINA MEDICAL JOURNAL whose terms expired this year were Dr. Reece Berryhill, dean of the University of North Carolina Medical School, and Dr. Josiah C. Trent of the Duke University School of Medicine, who was elected last January to fill the unexpired term of the late Dr. Frederic M. Hanes. Both these members were re-elected without opposition. Dr. Ernest W. Furgurson of Plymouth was elected by the editorial board to serve out the unexpired term of the late Dr. Paul P. McCain. Dr. Furgurson's choice is a happy one. He is a veteran and is one of the younger members of the Society who have evinced an interest in medical writing. He is just the sort of young man who can and should take an active part in the affairs of the Society. No doubt he will be a valuable addition to the editorial board.

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Mr. Edmund H. Harding of Washington lived up to his reputation as "The Tar Heel Humorist." He kept his audience spellbound with one story after another, and there was enough philosophy in his address to make it well worth while.

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The weather throughout the whole session was well nigh perfect. The only objection which might be offered was that it lured too many members away from the House of Delegates and the scientific sessions.

MEDICOLEGAL ABSTRACT

J. F. OWEN, M.D., LL.B.

RALEIGH

DEAD BODIES: *Unauthorized removal of portions of a dead body by one authorized to examine it, and his refusal to return such portions, on demand, to the surviving spouse or next of kin, is actionable.*

The plaintiff in this cause was the beneficiary under an accident insurance policy issued to her husband. He died under circumstances claimed to be accidental, and at the request of the insurance company the plaintiff authorized an autopsy. Two physicians representing the widow were secured for the purpose of witnessing the autopsy. They were present during the postmortem examination, and assumed responsibility for her interest at that time.

The plaintiff charged, and it was proved in the trial court, that the pathologist removed the heart, one kidney, and the brain for further study and failed to return them at the completion of the autopsy. There was a demand on the part of the widow for possession of the organs, but this was refused by the doctor who performed the examination. The court assumed that the physicians representing the widow had consented to the removal of the organs, but instructed the jury that the demand of the widow counteracted this consent by agency, and that the act upon the part of the defendant was actionable.

The jury awarded the widow the sum of $1500.00 in damages. This award was made upon the basis of mental anguish as alleged in the complaint. The defendant immediately appealed the case to the Circuit Court of Appeals.

When the case came up to be heard by the appellate court, this tribunal was of the opinion that the findings of the trial court should be sustained. In this connection the court stated that "a surviving spouse is entitled to the custody of a deceased person for the purpose of preservation and burial, and may maintain an action for damages against anyone who unlawfully and without authority mutilates or destroys such bodies. The authority to perform an autopsy includes acts and operations necessarily involved therein. It contemplates the removal of the internal organs, but does not contemplate their retention."

Strictly speaking, the law would appear to prohibit the retention of tissue even for microscopic study. The law has been said to be "nothing if not reasonable," and as a certain amount of tissue is essential for minute study, legal restrictions would not be expected to interfere with such an important source of information—provided, of course, that only the amount of material reasonably necessary for this purpose is removed and retained.

As a precaution, in securing permission for autopsies, a full explanation should be furnished the person who is authorizing the autopsy. The likelihood of litigation is thus lessened, and the physician-family relationship is usually maintained.

(District Court, S.D. Cal., N.D., March, 1933. V. 3., Federal Supplement, p. 358)

BULLETIN BOARD

PRESIDENT'S MESSAGE

ISAAC HALL MANNING

In the annals of medicine and medical education in North Carolina the name of Isaac Hall Manning will be awarded a position of eminence that time will not efface. It is fitting that those of us who knew him well should dedicate this issue of our JOURNAL to his memory. Too often contemporaries of great men neglect to record adequately their appreciation and esteem of their colleagues, but leave this opportunity to future historians.

There are few members of our Society, I am sure, who knew Dr. Manning intimately in so many capacities as I. When I was a medical student, I learned to love him as a teacher of physiology. Three years later, as resident physician at the University Infirmary, I knew him as a careful and skillful doctor. Then, in later years, while he was president of the Medical Society and director of the Hospital Saving Association, I came to respect him in the unusual role of medical sociologist. He remained actively engaged in medical endeavors until the very end of his useful career.

Medical students of the University during the period from 1913 to 1939 had the splen-

did experience of being exposed to the influence of four great men whom Dr. George Carrington has called "The Four Horsemen" —Drs. Manning, MacNider, Mangum, and Bullitt. During most of these years Dr. Manning served as dean. These men were able, through thorough medical teaching and by maintaining proper relationships with other institutions, to keep the University of North Carolina highly regarded in medical education. Dr. Manning, like all the others, dreamed of the day when the people of this state would elect to furnish to its citizens a complete medical education. The knowledge of this decision was denied him. Now that the people have elected to do so, his spirit, along with those of his colleagues who survive him, will act as a guiding light to those of us in the Society who seek to make the University School a complete and distinguished medical institution.

Dr. Manning's outstanding trait of character was his rugged honesty. Students soon learned this. His friends all accepted it. He never indulged in sycophancy or adulation. A word of praise from him could always be accepted as well deserved.

In his later years he became much interested in one of medicine's primary problems —better and more widespread hospitalization. His ideas in this regard constituted a basis upon which our medical care program is founded. He maintained that better medical care for the people depends upon better hospital service. Insurance, he insisted, is the answer to medical costs. In this respect his thinking was in advance of most medical men of that day.

Nothing gives me more pleasure, as one of "his boys," than to attest to his eminence as a teacher, his skill as a doctor, and his distinction as a medical economist. It must be left to someone more able than I to write a detailed statement of his value to his university and his state, but it is my fervent hope that it will be done.

Isaac Hall Manning, coming from an illustrious North Carolina family, was a great North Carolinian. His memory must be perpetuated. His contributions to medical education and medical care within the state were outstanding. The Medical Society of the State of North Carolina is honored in dedicating this number of its JOURNAL as a testimony of its love and respect for him.

W. M. COPPRIDGE, M.D.

NEWS NOTES FROM THE UNIVERSITY OF NORTH CAROLINA

Drs. C. D. Van Cleave and A. V. Jensen attended the meeting of the American Association of Anatomists in Montreal on April 3, 4, and 5. Dr. Jensen presented a paper entitled "Effect of Intermittent Exposure to 30,000 Feet Simulated Altitude on Brain Structure." This paper was written by Dr. Jensen in collaboration with Dr. William F. Windle.

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Dr. Cornelius T. Kaylor, assistant professor of anatomy at the University of Syracuse School of Medicine, has been appointed associate professor of anatomy and will assume his new duties in the summer.

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Dr. Kenneth M. Brinkhous, professor of pathology, presented a paper entitled "Thrombin and Its Clinical Applications" at the Southeastern Surgical Congress Postgraduate Assembly in Louisville, Kentucky, on March 10.

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On January 22 more than 150 medical alumni attended a memorial luncheon at the Carolina Inn held in honor of the late Dr. I. H. Manning, former dean and Kenan Professor Emeritus of Physiology. Dr. George Carrington, of Burlington, president of the Alumni Association, presided, and tributes were paid to Dr. Manning's contributions to medicine by Drs. W. R. Stanford and Paul F. Whitaker, President Graham, and Chancellor House. Mrs. I. H. Manning, Sr., and her three sons, Dr. I. H. Manning, Jr. and Messrs. John and Howard Manning were present.

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Dr. Edward G. M. McGavran, professor of public health and preventive medicine of the University of Kansas School of Medicine, has been appointed dean of the University of North Carolina School of Public Health to succeed the late Dr. Milton J. Rosenau and Acting Dean Herman G. Baity. He will also be head of the Department of Epidemiology. Dr. McGavran received his A.B. degree from Butler University in 1924, his M.D. from Harvard in 1928, and his M.P.H. from the Harvard School of Public Health in 1935.

Dr. McGavran has served as Director of Health and County Health Officer in Hillsdale, Michigan, for the W. K. Kellogg Foundation, as Health Commissioner of St. Louis County, Missouri, and Director of the West Virginia Public Health Training Center and Monogalia County Health Department at Morgantown, in each of which positions he has developed training centers for public health workers. He is also interested in research in tropical diseases and has carried on work for the Rockefeller Foundation in this field in Egypt, India, Hawaii, and Central America. Prior to going to Kansas, Dr. McGavran was on the faculty of the Washington University Medical School and acting head of the Department of Public Health and Preventive Medicine.

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Mr. Paul D. Haney has been appointed associate professor of sanitary engineering of the School of Public Health, beginning March 12, 1947. Mr. Haney received his B.S. in chemical engineering from the University of Kansas in 1933, and his M.S. in sanitary engineering from Harvard University, 1937. From 1942 until his arrival at the University, Mr. Haney was Director and Chief Engineer, Division of Sanitation, Kansas State Board of Health and associate professor of sanitary engineering, University of Kansas. Prior to that he was granted a leave of absence to accept a temporary commission in the U. S. Public Health Service. He was assigned to the Ohio River Pollution Survey.

Dr. H. G. Baity, acting dean and professor of sanitary engineering of the School of Public Health, attended the meeting of the Association of Schools of Public Health in Boston, Massachusetts, on April 9.

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Dr. Harold J. Magnuson, research professor of experimental medicine in the School of Public Health, attended the symposium, Recent Advances in the Investigation of Venereal Diseases held in Washington, D. C., on April 17, under the auspices of the Syphilis Study Section of the National Institute of Health. Dr. Magnuson presented two papers, entitled "The Rate of Development and Degree of Acquired Immunity in Experimental Rabbit Syphilis" and "The Minimal Infectious Inoculum of S. Pallida (Nichols Strain), and a Consideration of its Rate of Multiplication **in Vivo.**"

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The Department of Public Health Nursing, School of Public Health, University of North Carolina, announces a change in the curriculum leading to a certificate in public health nursing.

Beginning September, 1947, the curriculum will consist of three quarters of academic work, plus one quarter of field work.

In addition to the certificate program, the School of Public Health offers a Bachelor of Science degree in public health nursing. The School of Public Health also offers an M.P.H., or a Master's degree may be obtained in sociology or education.

News Notes from the Duke University School of Medicine

Dr. W. Henry Hollinshead, professor of anatomy, has accepted an appointment as professor of anatomy at the Mayo Foundation and Graduate School of Medicine, University of Minnesota, Rochester, Minnesota. In this position he will organize and head a Department of Anatomy which is being established by the Mayo Clinic and will continue his research upon the peripheral nervous system and mechanisms in the reflex control of respiration and blood pressure.

Dr. Hollinshead is one of the original staff of the Duke University School of Medicine, having been a member of the Department of Anatomy since 1930. He will assume his new duties July 1.

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The Department of Medicine has recently added to its staff the following members:

Dr. John Hickam, graduate of Harvard Medical School in 1940, house officer at Peter Bent Brigham Hospital 1940-1942, resident in medicine at Grady Hospital (Emory) 1942-1943, member of the Medical Corps of the Army of the United States 1943-1946, and research fellow of the American College of Physicians (Emory) 1946-1947.

Dr. Frank L. Engel, graduate of Johns Hopkins in 1938, house officer at Mount Sinai Hospital, New York 1938, National Research Council fellow in physiological chemistry at Yale 1941-1943, research assistant in physiological chemistry at Yale 1943-1945, associate in medicine at Emory, 1945-1947.

Dr. J. P. Myers, graduate of Stanford Medical School in 1937, house officer in medicine at Stanford University Hospitals 1936-1938, research fellow at Harvard, 1938-1939, assistant resident and resident at Peter Bent Brigham Hospital 1939-1942, Chief of General Medicine Section at 8th General Hospital (Harvard Unit) U. S. Army 1942-1944, and of 163rd General Hospital 1944-1945, associate in medicine at Emory, 1946-1947.

News Notes from the State Board of Health

Pulmonary tuberculosis, the leading cause of death among the communicable diseases, was responsible for 1,065 deaths in 1946 as compared to 1,287 for 1945, thereby establishing a new low. Pertussis, another major cause of death among the communicable diseases, showed the lowest number of both cases and deaths in the history of the state, except for the year 1936. Pertussis cases totaled 3,394 and deaths 57. Diphtheria, the next most important communicable disease insofar as deaths are concerned, caused fewer cases than ever before, but the number of deaths did not drop as low as the previous record. The 1946 cases were 590 in number as compared to 1,375 the previous year and 665 for 1944, the best year on record up to that time. Diphtheria deaths reported to date for 1946 numbered 53 as compared to 35 for 1944. Typhoid fever continued to decline as a public health problem. Only 54 cases were reported during the past year.

Malaria among returning service men has been reported frequently, but there appears to have been no appreciable spread to the civilian population. Cases for 1946 totaled 369 as compared to 554 the previous year. The chief communicable disease problem in the state that might be considered as war-connected is that of syphilis. In 1946 there were reported 2,452 cases of primary and secondary syphilis among males as compared to 1,522 the preceding year. There has been a corresponding increase among females—2,121 cases for 1946 and 1,550 for 1945.

Rocky Mountain spotted fever continued a twelve-year upward trend during 1946. There were 66 cases and 21 deaths reported. Endemic typhus fever, which had shown a ten-year upward trend in 1944 and was expected to continue upward in the southeastern United States, has declined in the past two years.

One new communicable disease problem made its appearance in this state during 1946. An outbreak of epidemic ringworm of the scalp was called to the attention of health officials in Alamance county by Dr. Callaway of Duke Hospital. Approximately 300 cases of this disease have been located in the area.

The past year brought a record number of births; preliminary estimates give a total of well over 100,000. The birth rate of 26.3 per 1,000 population is the highest recorded since 1928. The crude death rate of 7.6 deaths per 1,000 population is the lowest ever recorded in North Carolina. The maternal and infant death rates have both continued to decline.

The ten leading causes of death for 1946 show no change over 1945 and are as follows:

1. Heart disease
2. Intracranial vascular lesions
3. Nephritis
4. Cancer
5. Congenital malformations, prematurity, and neonatal diseases
6. Pneumonia
7. Violent deaths and non-vehicular accidents
8. Pulmonary tuberculosis
9. Automobile accidents
10. Other diseases of the digestive system.

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An important preparedness conference was held in Goldsboro on April 3, when representatives of various cooperating agencies met to plan for immediate mobilization in the event of any future outbreak of infantile paralysis anywhere in North Carolina. Among those participating were representatives of the National Foundation, the State Board of Health, local health units, and Parent-Teacher Association units, private physicians,

nurses, health educators, municipal officials, and various others. North Carolina doctors who took part on the program were Dr. Eric Bell, Dr. Carl Reynolds, Dr. Arthur London, Dr. William H. Roberts, Dr. George D. Wilson, and Dr. S. B. McPheeters.

News Notes from the North Carolina Tuberculosis Association

The annual meeting of the North Carolina Tuberculosis Association was held in Goldsboro on May 1 and 2. Among the North Carolina doctors participating were Dr. Hillis L. Seay, Dr. H. B. Ivey, Dr. H. Stuart Willis, and Dr. R. L. Carlton.

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Dr. W. D. Rodgers of Warrenton has been named a member of the executive committee of the Warren County Tuberculosis and Health Association.

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Dr. A. L. O'Briant of Raeford has been appointed a member of the Hoke County Tuberculosis Association.

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The North Carolina Tuberculosis Association and the Division of Vocational Rehabilitation have agreed upon principles of cooperation requisite to a united approach to the development of maximum vocational rehabilitation opportunities for persons with a history of tuberculosis.

Fifth District Medical Society

The Fifth District Medical Society met in Southern Pines on April 17. Speakers at the afternoon session were Dr. William Dosher of Wilmington, Dr. W. B. Bradford of Charlotte, Dr. Rowland F. Ziegler of Florence, S. C., and Drs. W. L. Thomas and R. A. Ross of the Duke University School of Medicine. Dr. Oren Moore of Charlotte gave the address at the dinner meeting.

Dr. C. O. Bristow of Rockingham is president of the Fifth District Society.

Ashe-Watauga Counties Medical Society

Dr. C. T. Jones of West Jefferson reported a case of "Multilocular Pseudomucinous Cystadenocarcinoma" at the meeting of the Ashe-Watauga Counties Medical Society on April 16. At the business meeting which preceded the scientific session, the constitution and by-laws of the new society were presented and adopted.

Catawba Valley Medical Society

A regular meeting of the Catawba Valley Medical Society was held on April 16 in Morganton. The program consisted of papers by Dr. A. M. Lang, Dr. G. N. Billings, and Dr. John Reece.

Edgecombe-Nash Counties Medical Society

The Edgecombe-Nash Counties Medical Society held its April meeting in Rocky Mount on April 9. Dr. P. T. Meyers of Kinston discussed "Cancer Prevention," and presented some movies.

Forsyth County Medical Society

Dr. J. Warrick Thomas of Richmond, Virginia, was guest speaker at the April meeting of the Forsyth County Medical Society, held in Winston-Salem on April 8. His subject was "The Handling of Certain Allergic Problems as Medical Emergencies."

Halifax County Medical Society

The Halifax County Medical Society met in Roanoke Rapids on April 11. The program consisted of a talk on "Allergy in General Practice" by Dr. W. Randolph Graham of Richmond, Virginia.

News Notes

Dr. J. D. Gilland, Jr., of Charlotte has recently moved to Kingstree, South Carolina, where he is continuing the practice of general surgery, and is director of surgery at the Kelley Memorial Hospital.

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Dr. Horace H. Hodges has announced the opening of offices in Charlotte for the practice of internal medicine and gastroenterology. He is associated with Dr. Monroe T. Gilmour.

American Congress on Obstetrics and Gynecology

The Third American Congress on Obstetrics and Gynecology, September 8-12, 1947, in St. Louis has scheduled three panel-type morning sessions on the following subjects:

(1) **Anesthesia and Analgesia**, Tuesday, September 9, Dr. Nicholas J. Eastman, chairman, with the cooperation of Dr. J. P. Greenhill, Chicago; Dr. John Adriani, New Orleans; Dr. Stuart Cullen, Iowa City; and Dr. Arthur Baptisti, Hagerstown.

(2) **Cancer**, Wednesday, September 10, Dr. Robert A. Kimbrough, Philadelphia, chairman, with the cooperation of Dr. John Randall, Iowa City; Dr. Charles L. Martin, Dallas; Dr. Joe V. Meigs, Boston; and Dr. Herbert Schmitz, Chicago.

(3) **Cesarean Section** on Thursday, September 11, Dr. Edward Schumann, Philadelphia, chairman, with the cooperation of Dr. Edward G. Waters, Jersey City; Dr. Edward Davis, Chicago; Dr. E. D. Plass, Iowa City; and Dr. William Benbow Thompson, Hollywood.

The afternoon meetings of the medical section of the Congress will consider the psychosomatic aspects of pregnancy on Tuesday; pregnancy complicated by heart disease, diabetes and tuberculosis on Wednesday; and recent advances in endocrinology on Thursday.

American Board of Obstetrics and Gynecology, Inc.

The general oral and pathology examinations (Part II) for all candidates will be conducted at Pittsburgh, Pennsylvania, by the entire Board from Sunday, June 1, through Saturday, June 7, 1947. The Hotel William Penn in Pittsburgh will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Hotel William Penn.

Candidates in military or naval service are requested to keep the secretary's office informed of any change in address.

Applications are now being received for the 1948 examinations. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

(BULLETIN BOARD CONTINUED ON PAGE 329)

AUXILIARY

OUR TUBERCULOSIS ASSOCIATIONS

Health is a priceless possession for an individual. Freedom from contagious disease is one of the greatest assets a community can possess.

A disease which is spread from person to person becomes a matter of public concern, because even one case is a potential threat to the entire community. One person with a contagious disease may give it to one, two, or more other persons, who in turn may pass it on to still others until scores may fall victim to the disease.

This is the reason that communities insist that cases of contagious diseases be reported to the health authorities. The greatest aid to health authorities in preventing the spread of a contagious disease is its early recognition. If the disease is discovered immediately, precautions can be taken to prevent others from coming in contact with the patient and thus possibly catching the disease.

There is one contagious disease which, unfortunately, is seldom recognized in its early stage. It is tuberculosis. This disease, which kills more young people between 13 and 35 than any other disease, frequently reaches an advanced stage before unmistakable symptoms appear. Meanwhile, however, the disease may be caught by others. Meanwhile, too, the individual may be losing his health, for the chances of recovery from tuberculosis are greatest when the disease is found early.

Even tuberculosis, however, can be found early through means of chest x-rays. If every adult had periodic chest x-rays, every new case of the disease would be found early, before the individual had lost his own health and before he had spread the disease to others.

Because of the danger which tuberculosis presents to the individual and to the community, our national, state, county and city tuberculosis associations were formed years ago to spread information about the disease and how it can be controlled.

The task of these associations is to find cases of tuberculosis, to find them in that early, most easily curable stage; to disseminate information about the nature of the disease and what steps can be taken to prevent its spread; to demonstrate the need for establishing and maintaining adequate facilities for detecting tuberculosis and for caring for its victims.

Such tasks may be undramatic, but they are necessary. If tuberculosis is to be brought under complete control in our communities, these associations will need our loyal support.

MRS. S. S. SAUNDERS,
Press and Publicity Chairman,
High Point

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Last Call for reservations for the Twenty-fourth Annual Convention of the Woman's Auxiliary to the American Medical Association, which will be held at Haddon Hall Hotel, Atlantic City, New Jersey.

ATLANTIC CITY EXTENDS A HEARTY WELCOME TO YOU

The physician and the public must be constantly impressed to respect and treat tuberculosis as a highly contagious disease. Margery Blahd, Eleanor I. Leslie, and Sol Roy Rosenthal, Am. Jour. Pub. Health, July, 1946.

The general hospital plays a very important role in the organization for the fight against tuberculosis inasmuch as it offers facilities necessary to tie together the agents of research, prevention and treatment. But many general hospitals refuse admission to patients afflicted with pulmonary tuberculosis and many insist upon the removal of patients whenever diagnostic study discloses the presence of this disease. Public health education has accomplished much by way of removing the barriers of prejudice which formerly restrained general hospitals from accepting tuberculosis patients and modern methods in the control of infection have made possible a certain degree of intercommunication among patients with various types of illness without danger of cross-infection. Consequently, it is entirely feasible for general hospitals knowingly to accept for treatment patients suffering from pulmonary tuberculosis.—Hospital Survey News Letter, Feb., 1946.

Infection with tuberculosis may be compared to the action of an incendiary bomb. It may come to rest in any isolated area of the body, generally first in the upper respiratory passages, and then may quickly be dispersed to other areas, like the bomb fragments causing incendiary fires.

The germ of tuberculosis may reproduce rapidly and set up secondary zones of inflammation and disease. Treatment is essentially like the suppression of the bomb. Nature assists in the process in trying to wall off the germ and build up a wall around it which isolates it from oxygen and other food nutriments brought to it by the blood stream. Putting out the fire of tuberculosis demands early finding of the infection and a mustering of all body forces of resistance to put out the fire in the same manner as the community would deal with an incendiary bomb.—Health and Safety Medium, Feb., 1946.

BOOK REVIEWS

Peripheral Vascular Diseases. By Edgar V. Allen, M.D., M.S., in Medicine, F.A.C.P., Division of Medicine, Mayo Clinic, Assoc. Prof. Medicine, Mayo Foundation, Graduate School, Univ. Minnesota; Diplomate of the American Board of Internal Medicine; and Nelson W. Barker, M.D., M.S. in Medicine, F.A.C.P., Division of Medicine, Mayo Clinic, Assoc. Prof. Medicine, Mayo Foundation, Graduate School, Univ. Minnesota; Diplomate of the American Board of Internal Medicine; and Edgar A. Hines, Jr., M.D., M.S. in Medicine, F.A.C.P., Division Medicine, Mayo Clinic, Assoc. Prof. Medicine, Mayo Foundation, Graduate School, Univ. Minnesota; with associates in the Mayo Clinic and Mayo Foundation. 871 pages, with 386 illustrations, 7 in color. Price, $10.00. Philadelphia and London: W. B. Saunders Company, 1946.

A consideration of peripheral vascular disease should not limit itself simply to diseases of the peripheral arterial system. Such a concept has been all too common in the past. The peripheral vascular system is composed of three separate sets of vessels—arteries, veins, and lymphatics. This book considers all of these components of the peripheral vascular system and discusses the diseases of each of them individually and in their relationship to each other. This is one of the prime reasons for its excellence. It discusses the gross and microscopic anatomy of peripheral blood vessels, as well as the approaches to the diagnosis of vascular diseases. Special methods of investigation are given in detail.

The excellent discussions of the disorders involving the peripheral arteries include not only those lesions which arise apparently in the arteries themselves, but also those diseases which arise in neighboring structures and involve the arteries secondarily. Included in this section are excellent chapters on tumors of the blood and lymph vessels. Disorders of the venous and lymphatic vessels are considered extensively and in detail. For all of these abnormalities, both medical and surgical treatments are thoroughly discussed.

The book is comprehensive in its scope and gives the specific details for conducting practically all of the special tests and examinations which are now used for the accurate diagnosis of peripheral vascular disease. Discussions of the various forms of treatment are likewise given in splendid detail.

The authors have combined excellent and extensive reviews of the literature with the result of their own experiences in the Mayo Clinic. One of the most valuable features of this work is the frank expression of the authors' honest opinion about the various measures used in diagnosing and treating peripheral vascular lesions.

This is by far the best and most inclusive work yet published on peripheral vascular disease. It should prove invaluable as a text and reference source.

Bacterial Chemistry and Physiology. By John Roger Porter, Associate Professor, Department of Bacteriology, College of Medicine, State University of Iowa. 1072 pages. Price, $12.00. New York: John Wiley and Sons, Inc., 1946.

This is an excellent book for anyone interested in biology to have available. The general discussions of bacterial metabolism constitute a very good review of the principles of biochemistry. A great deal of practical information is given both in the text and in the many detailed tables, while copious references to the literature lead to further pertinent information on practically all topics discussed. It is certainly to be recommended to anyone working with microorganisms and also to anyone wishing to review biochemistry in a pleasant way.

The Personality of the Preschool Child. By Werner Wolff, Ph.D., Professor of Psychology, Bard College. 341 pages. Price, $5.00. New York: Grune & Stratton, 1946.

Dr. Wolff has presented a controversial subject in an unusually clear manner.

He has emphasized the need of approaching the preschool child in a dynamic way. He explains logically the reason that such objective tests as the Binet-Simon intelligence test may not give a true picture of the child's potentialities. Many of children's behavior disorders can be traced to aberrations in what Dr. Wolff calls, "the child's search for his self."

Discussion of the significance of children's drawings makes up a large part of the book. Considerable importance has been attached to the interpretation of these pictures, and the explanations of the interpretations are exceptionally clear and interesting.

This book should be of interest to anyone concerned with either normal or abnormal child development. Pediatricians would find this book of theoretical value, and intelligent parents might understand better their children's behavior.

In Memoriam

James M. Judd, M.D.

Dr. James M. Judd, a beloved pioneer civic leader of Wake County, was born in Wake County, January 29, 1871, and died at his home in Varina, March 7, 1947. He was graduated from the Baltimore Medical College in 1897. He was licensed to practice medicine in the state of North Carolina the same year. He began his medical career in lower Wake County, near what is now Varina.

At the time Dr. Judd began practicing medicine in North Carolina there were no good roads, no automobiles, no telephones, and the quickest way to get a physician was by horseback. At that time lower Wake County was practically a wilderness.

Dr. Judd was ever a true friend to the poor, and showed the same faithful, capable, and courteous service to every patient. A patient's financial status did not influence the quality of attention that Dr. Judd gave. He lived a full, useful and successful life. In addition to his professional career he was a true civic pioneer and leader, always interested in improving the social, religious and living conditions in his community. He was a successful farmer. He was one of the organizers of the Bank of Varina and was its president until his death. He built and operated a small hosiery mill. He was an active and influential member of the Methodist Church and a liberal contributor.

Dr. Judd has not left his community without a physician. His son, Dr. Glenn Judd, is a most useful and capable young physician who is carrying on the work his father began nearly half a century ago.

In Dr. Judd's death Wake County has lost one of its most useful citizens, the church a faithful and useful member, and the medical profession a valuable member. Our sympathy goes out to the members of his family.

Respectfully submitted,
John B. Wright, M.D.
Verne S. Caviness, M.D.
Committee, Wake County Medical Society

April 10, 1947

* * * *

George Stephenson Coleman, M.D.

Dr. Coleman was born in Pasquotank County, July 4, 1880, the son of Henry Butler Coleman and Louisa Brigman Coleman. He studied medicine at the Medical College of Virginia, from which he was graduated in 1907. He secured a license to practice medicine in North Carolina and began his practice at Kenly in the same year. He joined the State Medical Society the following year and remained an active and interested member of organized medicine throughout the remainder of his life.

During World War I, Dr. Coleman served overseas for two years with the 81st Division, with the rank of captain. In 1933 he left Kenly to take a position in Raleigh as Medical Director of the State Prison. He held this position for four years. After completing postgraduate studies in proctology in Atlanta, New Orleans, and the Mayo Clinic, he began the private practice of proctology in Raleigh in 1937.

Until the time of his death Dr. Coleman was a member of the staffs at Rex Hospital, St. Agnes Hospital, and Dix Hill. He was a faithful member of the Edenton Street Methodist Church, and throughout his life took a deep interest in civic and fraternal affairs. He was always deeply interested in organized medicine and was frequently a delegate to the State Medical Society meetings. He was president of the Johnson County Medical Society while practicing in Kenly, and after moving to Raleigh he was elected president of the Wake County Medical Society. He was scrupulously careful of his medical ethics and made it a rule to speak ill of no one.

In his death we experienced a deep loss. Our sympathy goes out to the members of his family.

Respectfully submitted,
John B. Wright, M.D.
Verne S. Caviness, M.D.
Committee, Wake County Medical Society

April 10, 1947

New Salt Substitute Developed by Winthrop

People who cannot or should not use salt may now at least have the savor. Meeting newest medical concepts of salt-free diets, scientists of the Winthrop Chemical Company, Inc., have developed a new salt substitute. Called Neocurtasal, the product will be sold in retail drug stores, according to Dr. Theodore G. Klumpp, Winthrop's president.

The new product contains no sodium. It has a salty flavor, however, is palatable, flows freely, and is used in the same manner as salt. It is being distributed in 2-ounce shakers and 8-ounce bottles. The product is described as "odorless, white, crystalline, some hygroscopic powder, consisting of potassium chloride, ammonium chloride, potassium formate, calcium formate, magnesium citrate and starch."

BULLETIN BOARD

(CONTINUED FROM PAGE 326)

Nursing Council Seeks Answer to Shortage of Registered Nurses

As a basic step in overcoming the acute shortage of registered nurses and other problems in the field, the National Nursing Council, representing fourteen leading professional organizations, is undertaking an intensive study of the registered nurse's real job and the changes in education that she requires for it. The study is being financed by a grant of approximately $28,000 from the Carnegie Corporation of New York.

Conference on Cerebral Palsy

At the first conference of its kind, specialists working with children with cerebral palsy—"spastics"—met at the U. S. Children's Bureau, Social Security Administration, Federal Security Agency, March 26-28, and pooled their experience preparatory to a major effort by the Bureau and state crippled children's agencies to get help to these "tragically neglected children."

This contemplated expansion of services to children with cerebral palsy is in line with a general expansion of services to crippled children made possible with the increased federal funds for this work with crippled children, authorized last August under amendments to the Social Security Act. State agencies, which are responsible for administration of these programs under plans approved by the Children's Bureau, now have on their lists the names of more than 40,000 children with cerebral palsy.

American Heart Association

The appointment of Dr. Charles A. R. Connor as associate medical director of the American Heart Association was announced recently by Dr. Howard F. West, president of the Association.

Dr. Connor will work with Dr. David D. Rutstein, medical director, in the development of the Association's program of research, service and public education in diseases of the heart and circulation.

Rheumatic Fever Library

The Colorado Rheumatic Fever Library has been established at the University of Colorado School of Medicine in response to the great need for the assembling in one place of all that has been written on the subject of rheumatic fever. It is desired that this library contain reprints or copies of every article that has been written on rheumatic fever.

At first efforts will be made to collect all of the reprints that may be available, and when reprints can no longer be obtained, photostatic or typewritten copies of desired articles will be made. Publications, or copies thereof, from countries outside of the United States will be collected in a similar manner and where necessary will be translated. This material will be cross-indexed and assembled in bound volumes by years. The collection will ultimately be made available to all workers in the field of rheumatic fever in the form of a photostat and an abstract service. It is hoped that this body of information, readily available to all interested persons, will form a major contribution to the solution of the basic problems of etiology and therapy of rheumatic fever.

Valuable assistance can be given by all libraries, all medical journals, all those writing in the field of rheumatic fever and all those willing to dispose of reprint collections by contributing papers relating to rheumatic fever, as well as by making a practice of sending reprints of future publications.

American Pharmaceutical Manufacturers' Association

The new annual Research Award of the American Pharmaceutical Manufacturers' Association was presented for the first time when the Association assembled for its fortieth annual meeting on April 28 at Boca Raton, Florida. Dr. Bernardo Alberto Houssay of Buenos Aires, Argentina, was the first recipient.

Dr. Houssay, who until recently was professor of physiology at the Medical School of the University of Buenos Aires, a post which he first assumed in 1919, is an authority on the inter-relationships of the various hormones. He is particularly noted for furthering medical knowledge of the pituitary gland, the "master" gland of the body. It was through Dr. Houssay's work that the relation of the pituitary gland to diabetes was firmly established.

Veterans Administration

The number of veterans awaiting hospitalization in Veterans Administration hospitals has declined 21 per cent in the last eight months, VA reported recently. The reduction resulted from the acquisition of "surplus" military hospitals, increasing the number of beds available for veterans, and from the more rapid turnover of patients in VA hospitals through improved medical care.

On July 1, 1946, there were 29,450 veterans on VA hospital waiting lists, whereas, on March 1, 1947, the figure had fallen to 23,200—a drop of 6,250 veterans, or 21 per cent.

United Service to China, Inc.

Forty-five of the 125 Chinese doctors, dentists, public health experts and nurses to whom fellowship awards will be made annually are now in this country engaged in advanced studies at leading American universities in fourteen states. Seven additional fellows are now **en route** to the United States.

The fellowship awards were bestowed by the American Bureau for Medical Aid to China, a cooperating agency of United Service to China, as part of a three-year program under which six national medical colleges in various parts of China will receive aid designed to elevate their standard of medical education to that of the best institutions in the United States.

ABMAC's new long-range program has been launched to help supply China's pressing need for more and better-trained medical and public health personnel. China has only about 13,000 qualified doctors for its 450 million population, and should have at least 266,000 if the Chinese people are to have anything approximating adequate medical care.

Second year woman medical student with considerable hospital laboratory experience desires summer employment. Registered technician. Camp employment will be considered also.

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